NEW ZEALAND DATA SHEET

1 PRODUCT NAME

LIBTAYO 350 mg/7mL concentrate for solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One mL of concentrate contains 50 mg of cemiplimab.

Each vial contains 350 mg of cemiplimab in 7 mL of solution.

Cemiplimab is produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture.

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate).

Clear to slightly opalescent, colourless to pale yellow solution with a pH of 6.0 and osmolality between 300 and 360 mmol/kg. The solution may contain trace amounts of translucent to white particles in a single-use vial.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

LIBTAYO has provisional consent (see section 5.1) for the indication below:

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

4.2 DOSE AND METHOD OF ADMINISTRATION

Treatment must be initiated and supervised by physicians experienced in the treatment of cancer.

Posology

Recommended dose

The recommended dose is 350 mg cemiplimab every 3 weeks (Q3W) administered as an intravenous infusion over 30 minutes. Treatment may be continued until disease progression or unacceptable toxicity.

Dose modifications

No dose reductions are recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability. Recommended modifications to manage adverse reactions are provided in Table 1.

Detailed guidelines for the management of immune-related adverse reactions are described in Table 1 (see also Section 4.4 and Section 4.8).

Table 1 - Recommended treatment modifications

Adverse Reaction[a]	Severity[b]	Dose modification	Additional intervention
Immune-Related Adverse Reactions			
Pneumonitis	Grade 2	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume LIBTAYO if pneumonitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue	Initial dose of 2 to 4 mg/kg/day prednisone or equivalent followed by a taper
Colitis	Grade 2 or 3	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume LIBTAYO if colitis or diarrhoea improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 4 or recurrent Grade 3	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Hepatitis	Grade 2 with AST or ALT >3 and ≤5×ULN or total bilirubin >1.5 and ≤3×ULN	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume LIBTAYO if hepatitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or returns to baseline AST or ALT after completion of corticosteroid taper	
	Grade ≥3 with AST or ALT >5×ULN or total bilirubin >3×ULN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Hypothyroidism	Grade 3 or 4	Withhold LIBTAYO	Initiate thyroid hormone replacement as clinically indicated
		Resume LIBTAYO when hypothyroidism returns to Grade 0 to 1 or is otherwise clinically stable	

Adverse Reaction[a]	Severity[b]	Dose modification	Additional intervention
Immune-Related Adverse Reactions			
Hyperthyroidism	Grade 3 or 4	Withhold LIBTAYO	Initiate symptomatic management
		Resume LIBTAYO when hyperthyroidism returns to Grade 0 to 1 or is otherwise clinically stable	
Hypophysitis	Grade 2 to 4	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume LIBTAYO if hypophysitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or is otherwise clinically stable	
Adrenal insufficiency	Grade 2 to 4	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume LIBTAYO if adrenal insufficiency improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or is otherwise clinically stable	
Type 1 diabetes mellitus	Grade 3 or 4 (hyperglycaemia)	Withhold LIBTAYO	Initiate treatment with anti-hyperglycaemics as clinically indicated
		Resume LIBTAYO when diabetes mellitus returns to Grade 0 to 1 or is otherwise clinically stable	
Skin adverse reactions	Grade 2 lasting longer than 1 week, Grade 3 or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume LIBTAYO if skin reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 4 or confirmed SJS or TEN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-related skin reaction or other immune-related adverse reactions in	Grade 2	Withhold LIBTAYO	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper

Adverse Reaction[a]	Severity[b]	Dose modification	Additional intervention
Immune-Related Adverse Reactions			
patients with prior treatment with idelalisib		Resume LIBTAYO if skin reaction or other immune-related adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 3 or 4 (excluding endocrinopathies) or recurrent Grade 2	Permanently discontinue	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Nephritis with renal dysfunction	Grade 2 creatinine increased	Withhold LIBTAYO	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume LIBTAYO if nephritis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 3 or 4 creatinine increased	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Other immune-related adverse reactions	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-related adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	

Adverse Reaction[a]	Severity[b]	Dose modification	Additional intervention
Immune-Related Adverse Reactions			
	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 Recurrent Grade 3 immune-related adverse reaction Persistent Grade 2 or 3 immune-related 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	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent as clinically indicated followed by a taper
Haemophagocytic lymphohistiocytosis (HLH)	Suspected	Withhold LIBTAYO	Initiate treatment
		Resume LIBTAYO at physician's discretion if diagnosis of HLH is excluded	
	Confirmed	Permanently discontinue	Initiate/continue treatment for HLH
Infusion-related reactions [a]			
Infusion-related reaction	Grade 1 or 2	Interrupt or slow rate of infusion	Initiate symptomatic management
	Grade 3 or 4	Permanently discontinue	

ALT: alanine aminotransferase; AST: aspartate aminotransferase; ULN: upper limit of normal.
[a] See also Warnings and Precautions (Section 4.4) and Adverse Reactions (Section 4.8)
[b] Toxicity should be graded with the current version of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE).

Patient Alert Card

All prescribers of LIBTAYO should be familiar with the educational materials and inform the patients about the Patient Alert Card explaining what to do should they experience any symptom of immune-related adverse reactions and infusion-related reactions. The physician will provide the Patient Alert Card to each patient.

Special populations

Paediatric population

The safety and efficacy of LIBTAYO in children and adolescents below the age of 18 years have not been established. No data are available.

Elderly

No dose adjustment is recommended for elderly patients. Cemiplimab exposure is similar across all age groups (see Section 5.1 and Section 5.2).

Renal impairment

No dose adjustment of LIBTAYO is recommended for patients with renal impairment. There are limited data for LIBTAYO in patients with severe renal impairment CL_{cr} 15 to 29 ml/min (see Section 5.2).

Hepatic impairment

No dose adjustment is recommended for patients with mild hepatic impairment. LIBTAYO has not been studied in patients with moderate or severe hepatic impairment. There are insufficient data in patients with moderate or severe hepatic impairment for dosing recommendations (see Section 5.2).

Method of administration

LIBTAYO is for intravenous use. It is administered by intravenous infusion over 30 minutes through an intravenous line containing a sterile, non-pyrogenic, low-protein binding, in-line or add-on filter (0.2 micron to 5 micron pore size).

Other medicinal products should not be co-administered through the same infusion line.

For instructions on dilution of the medicinal product before administration, see Section 6.6.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Immune-related adverse reactions

Severe and fatal immune-related adverse reactions have been observed with cemiplimab (see Section 4.2 and Section 4.8). These immune-related reactions may involve any organ system. Most immune-related reactions initially manifest during treatment with cemiplimab; however, immune-related adverse reactions can occur after discontinuation of cemiplimab.

Immune-related adverse reactions affecting more than one body system can occur simultaneously, such as myositis and myocarditis or myasthenia gravis, in patients treated with cemiplimab or other PD-1/PD-L1 inhibitors.

Monitor patients for signs and symptoms of immune-related adverse reactions. Immune-related adverse reactions should be managed with cemiplimab treatment modifications, hormone replacement therapy (if clinically indicated), and corticosteroids. For suspected immune-related adverse reactions, patients should be evaluated to confirm an immune-related adverse reaction and to exclude other possible causes, including infection. Depending upon the severity of the adverse reaction, cemiplimab should be withheld or permanently discontinued (see Section 4.2).

Immune-related pneumonitis

Immune-related pneumonitis, defined as requiring use of corticosteroids with no clear alternate aetiology, including fatal cases, has been observed in patients receiving cemiplimab (see Section 4.8). Patients should be monitored for signs and symptoms of pneumonitis and causes other than immune-related pneumonitis should be ruled out. Patients with suspected pneumonitis should be evaluated with radiographic imaging as indicated based on clinical evaluation and managed with cemiplimab treatment modifications and corticosteroids (see Section 4.2).

Immune-related colitis

Immune-related diarrhoea or colitis, defined as requiring use of corticosteroids with no clear alternate aetiology, has been observed in patients receiving cemiplimab (see Section 4.8) Patients should be monitored for signs and symptoms of diarrhoea or colitis and managed with cemiplimab treatment modifications, anti-diarrhoeal agents, and corticosteroids (see Section 4.2).

Immune-related hepatitis

Immune-related hepatitis, defined as requiring use of corticosteroids with no clear alternate aetiology, including fatal cases, has been observed in patients receiving cemiplimab (see Section 4.8). Patients should be monitored for abnormal liver tests prior to and periodically

during treatment as indicated based on clinical evaluation and managed with cemiplimab treatment modifications and corticosteroids (see Section 4.2).

Immune-related endocrinopathies

Immune-related endocrinopathies, defined as treatment-emergent endocrinopathies with no clear alternate aetiology, have been observed in patients receiving cemiplimab (see Section 4.8).

Thyroid disorders (Hypothyroidism/Hyperthyroidism)

Thyroid disorders have been observed in patients receiving cemiplimab. Thyroid disorders can occur at any time during the treatment. Patients should be monitored for changes in thyroid function at the start of treatment and periodically during the treatment as indicated based on clinical evaluation (see Section 4.8). Patients should be managed with hormone replacement therapy (if indicated) and cemiplimab treatment modifications. Hyperthyroidism should be managed according to standard medical practice (see Section 4.2).

Hypophysitis

Hypophysitis has been observed in patients receiving cemiplimab (see Section 4.8). Patients should be monitored for signs and symptoms of hypophysitis and managed with cemiplimab treatment modifications, corticosteroids and hormone replacement, as clinically indicated (see Section 4.2).

Adrenal insufficiency

Adrenal insufficiency has been observed in patients receiving cemiplimab (see Section 4.8). Patients should be monitored for signs and symptoms of adrenal insufficiency during and after treatment and managed with cemiplimab treatment modifications, corticosteroids and hormone replacement, as clinically indicated (see Section 4.2).

Type 1 Diabetes mellitus

Type 1 diabetes mellitus, including diabetic ketoacidosis, has been observed in patients receiving cemiplimab (see Section 4.8). Patients should be monitored for hyperglycaemia and signs and symptoms of diabetes as indicated based on clinical evaluation and managed with oral anti-hyperglycaemics or insulin and cemiplimab treatment modifications (see Section 4.2).

Immune-related skin adverse reactions

Immune-related skin adverse reactions, defined as requiring use of systemic corticosteroids with no clear alternate aetiology, including severe cutaneous adverse reactions (SCARs), such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) (some cases with fatal outcome), and other skin reactions such as rash, erythema multiforme, pemphigoid, have been reported in association with cemiplimab treatment (see Section 4.8).

Patients should be monitored for evidence of suspected severe skin reactions and exclude other causes. Patients should be managed with cemiplimab treatment modifications and

corticosteroids (see Section 4.2). For symptoms or signs of SJS or TEN, refer the patient for specialised care for assessment and treatment and manage patient with treatment modifications (see section 4.2).

Cases of SJS, fatal TEN and stomatitis occurred following 1 dose of cemiplimab in patients with prior exposure to idelalisib, who were participating in a clinical trial evaluating cemiplimab in Non-Hodgkin Lymphoma (NHL), and who had recent exposure to sulfa containing antibiotics (see Section 4.8). Patients should be managed with cemiplimab treatment modifications and corticosteroids as described above (see Section 4.2). For symptoms or signs of SJS or TEN, refer the patient for specialised care for assessment and treatment and manage patient with treatment modifications (see Section 4.2).

Immune-related nephritis

Immune-related nephritis, defined as requiring use of corticosteroids with no clear alternate aetiology, has been observed in patients receiving cemiplimab (see Section 4.8). Monitor patients for changes in renal function. Patients should be managed with cemiplimab treatment modifications and corticosteroids (see Section 4.2).

Other immune-related adverse reactions

Other fatal and life-threatening immune-related adverse reactions have been observed in patients receiving cemiplimab including paraneoplastic encephalomyelitis meningitis and myositis (see Section 4.8 for other immune-related adverse reactions).

Evaluate suspected immune-related adverse reactions to exclude other causes. Patients should be monitored for signs and symptoms of immune-related adverse reactions and managed with cemiplimab treatment modifications and corticosteroids as clinically indicated (see Section 4.2 and Section 4.8).

Cases of solid organ transplant rejection have been reported in the post-marketing setting with cemiplimab and other PD-1/PD-L1 inhibitors. Cases of graft-versus-host disease have been reported in the post-marketing setting in patients treated with other PD-1/PD-L1 inhibitors in association with allogeneic hematopoietic stem cell transplant.

Haemophagocytic lymphohistiocytosis (HLH) has been reported in the postmarketing setting with LIBTAYO (see Section 4.8). Patients should be monitored for clinical signs and symptoms of HLH. If HLH is suspected, administration of LIBTAYO should be withheld and treatment initiated (see Section 4.2). If HLH is confirmed, administration of LIBTAYO should be permanently discontinued.

Infusion-related reactions

Cemiplimab can cause severe or life-threatening infusion-related reactions (see Section 4.8). Patients should be monitored for signs and symptoms of infusion-related reactions and managed with cemiplimab treatment modifications and corticosteroids. Cemiplimab should be interrupted or the rate of infusion slowed for mild or moderate infusion-related reactions. The infusion should be stopped and cemiplimab should be permanently discontinued for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions (see Section 4.2).

Patients excluded from clinical studies

Patients that had active infections or that were immunocompromised were not included in the main study. For a full list of patients excluded from clinical trials, see Section 5.1.

In the absence of data, cemiplimab should be used with caution in these populations after careful evaluation of the balance of benefits and risks for the patient.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No pharmacokinetic (PK) drug-drug interaction studies have been conducted with cemiplimab.

The use of systemic corticosteroids or immunosuppressants before starting cemiplimab, except for physiological doses of systemic corticosteroid (≤10 mg/day prednisone or equivalent), should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of cemiplimab. However, systemic corticosteroids or other immunosuppressants can be used after starting cemiplimab to treat immune-related adverse reactions (see Section 4.2).

4.6 FERTILITY, PREGNANCY AND LACTATION

Women of childbearing potential

Women of childbearing potential should use effective contraception during treatment with cemiplimab and for at least 4 months after the last dose of cemiplimab.

Effects on fertility

No clinical data are available on the possible effects of cemiplimab on fertility. No effects on fertility assessment parameters (menstrual cycle and semen analysis) or male and female reproductive organs were observed in a 3-month repeat dose fertility assessment study with sexually mature cynomolgus monkeys at doses up to the highest dose studied of 50 mg/kg/week IV, resulting in exposures (AUC and C_{max}) approximately 20 times that expected in patients.

Use in pregnancy (Category D)

Animal reproduction studies have not been conducted with cemiplimab. There are no available data on the use of cemiplimab in pregnant women. As reported in the literature, PD-1/PD-L1 signalling pathway plays a role in sustaining pregnancy by maintaining immunological tolerance and animal studies have shown that PD-1 receptor blockade can result in an increase in fetal loss.

The increase of spontaneous abortion and/or resorption in animals with restricted PD-L1 expression (knock-out or anti-PD1/PD-L1 monoclonal antibodies) has been shown in both mice and monkeys. These animal species have similar maternal fetal interface to that in humans.

Human IgG4 is known to cross the placental barrier and cemiplimab is an IgG4; therefore, cemiplimab has the potential to be transmitted from the mother to the developing fetus. Cemiplimab is not recommended during pregnancy and in women of childbearing potential not using effective contraception unless the clinical benefit outweighs the potential risk.

Use in lactation

It is unknown whether cemiplimab is secreted in human milk. It is known that antibodies (including IgG4) are secreted in human milk; a risk to the breast-feeding newborn/infant cannot be excluded.

If a woman chooses to be treated with cemiplimab, she should be instructed not to breast-feed while being treated with cemiplimab and for at least 4 months after the last dose.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Cemiplimab has no or negligible influence on the ability to drive and use machines. Fatigue has been reported following treatment with cemiplimab (see Section 4.8).

4.8 UNDESIRABLE EFFECTS

Summary of the safety profile

Immune-related adverse reactions can occur with cemiplimab. Most of these, including severe reactions, resolved following initiation of appropriate medical therapy or withdrawal of cemiplimab (see *Description of selected adverse reactions* below).

The safety of cemiplimab has been evaluated in 591 patients with advanced solid malignancies including 219 advanced CSCC patients who received cemiplimab monotherapy in 2 clinical studies (R2810-ONC-1423 and R2810-ONC-1540). Of these 219 patients, 131 patients had mCSCC (nodal or distant) and 88 patients had laCSCC. Immune-related adverse reactions occurred in 20.3% of patients treated with cemiplimab in clinical trials including Grade 5 (0.7%), Grade 4 (1.2%) and Grade 3 (6.3%). Immune-related adverse reactions led to permanent discontinuation of cemiplimab in 4.4% of patients. The most common immune-related adverse reactions were hypothyroidism (7.1%), pneumonitis (3.7%), cutaneous adverse reactions (2.0%), hyperthyroidism (1.9%) and hepatitis (1.9%) (see *Description of selected adverse reactions* below, *Special warnings and precautions for use* in Section 4.4 and *Recommended treatment modifications* in Section 4.2). Adverse reactions were serious in 8.6% of patients and led to permanent discontinuation of cemiplimab in 5.8% of patients.

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with cemiplimab treatment (see Section 4.4).

Tabulated list of adverse reactions

Listed in Table 2 are adverse reactions by system organ class and by frequency. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to <1/1,000); very rare (< 1/10,000); not known (cannot be

estimated from available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 2 - Tabulated list of adverse reactions in patients treated with cemiplimab

System organ class preferred term	Grades 1-5 (Frequency category)	Grades 1-5 (%)	Grades 3-5 (%)
Immune system disorders			
Infusion-related reaction	Common	4.1	0
Sjogren's syndrome	Uncommon	0.5	0
Immune thrombocytopenic purpura	Uncommon	0.2	0
Vasculitis	Uncommon	0.2	0
Solid organ transplant rejection[a]	Not known	--	--
Endocrine disorders			
Hypothyroidism	Common	9.6	0
Hyperthyroidism	Common	2.7	0
Type 1 diabetes mellitus[b]	Uncommon	0.7	0.7
Adrenal insufficiency	Uncommon	0.5	0.5
Hypophysitis	Uncommon	0.5	0.5
Thyroiditis	Uncommon	0.2	0
Nervous system disorders			
Paraneoplastic encephalomyelitis	Uncommon	0.2	0.2
Chronic inflammatory demyelinating polyradiculoneuropathy	Uncommon	0.5	0
Encephalitis	Uncommon	0.5	0.5
Meningitis[c]	Uncommon	0.5	0.5
Guillain-Barre syndrome	Uncommon	0.2	0.2
Central nervous system inflammation	Uncommon	0.2	0
Neuropathy peripheral[d]	Uncommon	0.5	0
Myasthenia gravis	Uncommon	0.2	0
Eye disorders			
Keratitis	Uncommon	0.5	0
Cardiac disorders			
Myocarditis[e]	Uncommon	0.5	0.5
Pericarditis[f]	Uncommon	0.5	0.5
Respiratory, thoracic and mediastinal disorders			
Pneumonitis	Common	5.9	2.3
Gastrointestinal disorders			
Diarrhoea[g]	Very common	13.2	0.5

System organ class preferred term	Grades 1-5 (Frequency category)	Grades 1-5 (%)	Grades 3-5 (%)
Stomatitis	Common	2.4	0
Hepatobiliary disorders			
Hepatitis[h]	Common	1.4	1.4
Skin and subcutaneous skin disorders			
Rash[i]	Very common	23.3	1.4
Pruritus[j]	Very common	12.3	0
Musculoskeletal and connective tissue disorders			
Arthralgia	Common	5.0	0
Musculoskeletal pain[k]	Common	4.1	0.5
Arthritis[l]	Common	1.4	0.5
Muscular weakness	Uncommon	0.9	0
Polymyalgia rheumatica	Uncommon	0.5	0
Myositis[a]	Not known	--	--
Renal and urinary disorders			
Nephritis	Uncommon	0.5	0
General disorders and administration site conditions			
Fatigue[m]	Very common	21.5	0.9
Investigations			
Alanine aminotransferase increased	Common	5.5	0.5
Aspartate aminotransferase increased	Common	5.0	0.9
Blood alkaline phosphatase increased	Common	2.7	0
Blood creatinine increased	Common	1.8	0

Version 4.03 of NCI CTCAE was used to grade toxicity.

a. Post-marketing event
b. Type 1 diabetes mellitus is a composite term that includes diabetes mellitus, diabetic ketoacidosis and type 1 diabetes mellitus.
c. Meningitis is a composite term that includes meningitis and meningitis aseptic.
d. Neuropathy peripheral is a composite term that includes neuropathy peripheral and neuritis.
e. Myocarditis is a composite term that includes autoimmune myocarditis and myocarditis.
f. Pericarditis is a composite term that includes autoimmune pericarditis and pericarditis
g. Diarrhoea is a composite term that includes diarrhoea and colitis.
h. Hepatitis is a composite term that includes hepatitis and autoimmune hepatitis.
i. Rash is a composite term that includes rash maculo-papular, rash, dermatitis, rash generalised, dermatitis bullous, drug eruption, erythema, pemphigoid, psoriasis, rash erythematous, rash macular, rash pruritic and skin reaction.
j. Pruritus is a composite term that includes pruritus and pruritus allergic.
k. Musculoskeletal pain is a composite term that includes back pain, musculoskeletal pain, myalgia, neck pain and pain in extremity.
l. Arthritis is a composite term that includes arthritis and polyarthritis.
m. Fatigue is a composite term that includes fatigue and asthenia.

Description of selected adverse reactions

The selected adverse reactions described below are based on safety of cemiplimab in 591 patients in uncontrolled clinical studies.

Immune-related adverse reactions (see Section 4.2 and Section 4.4)

Immune-related pneumonitis

Immune-related pneumonitis occurred in 22 (3.7%) of 591 patients receiving cemiplimab, including 2 (0.3%) patients with Grade 5, 2 (0.3%) patients with Grade 4, and 6 (1.0%) patients with Grade 3 pneumonitis. Immune-related pneumonitis led to permanent discontinuation of cemiplimab in 11 (1.9%) of 591 patients. Among the 22 patients with immune-related pneumonitis, the median time to onset was 3.8 months (range: 7 days to 18 months) and the median duration of pneumonitis was 21.5 days (range: 5 days to 6.5 months). Eighteen patients (3.0%) received high-dose corticosteroids for a median of 8.5 days (range: 1 day to 5.9 months). Resolution of pneumonitis had occurred in 14 (63.6%) of the 22 patients at the time of data cut-off.

Immune-related colitis

Immune-related diarrhoea or colitis occurred in 7 (1.2%) of 591 patients receiving cemiplimab including 2 (0.3%) with Grade 3 immune-related diarrhoea or colitis. Immune-related diarrhoea or colitis led to permanent discontinuation of cemiplimab in 1 (0.2%) of 591 patients. Among the 7 patients with immune-related diarrhoea or colitis, the median time to onset was 3.8 months (range: 15 days to 6.0 months) and the median duration of immune-related diarrhoea or colitis was 30 days (range: 4 days to 8.6 months). Four patients (0.7%) with immune-related diarrhoea or colitis received high-dose corticosteroids for a median of 29 days (range: 19 days to 2.0 months). Resolution of immune-related diarrhoea or colitis had occurred in 4 (57.1%) of the 7 patients at the time of data cut-off.

Immune-related hepatitis

Immune-related hepatitis occurred in 11 (1.9%) of 591 patients receiving cemiplimab including 1 (0.2%) patient with Grade 5, 1 (0.2%) patient with Grade 4, and 9 (1.5%) patients with Grade 3 immune-related hepatitis. Immune-related hepatitis led to permanent discontinuation of cemiplimab in 5 (0.8%) of 591 patients. Among the 11 patients with immune-related hepatitis, the median time to onset was 1.0 month (range: 7 days to 4.2 months) and the median duration of hepatitis was 15 days (range: 8 days to 2.7 months). Ten (1.7%) patients with immune-related hepatitis received high-dose corticosteroids for a median of 10.5 days (range: 2 days to 1.9 months). Resolution of hepatitis had occurred in 8 (72.7%) of the 11 patients at the time of data cut-off.

Immune-related endocrinopathies

Hypothyroidism occurred in 42 (7.1%) of 591 patients receiving cemiplimab including 1 (0.2%) patient with Grade 3 hypothyroidism. No patient discontinued cemiplimab due to hypothyroidism. Among the 42 patients with hypothyroidism, the median time to onset was 4.2 months (range: 15 days to 18.9 months).

Hyperthyroidism occurred in 11 (1.9%) of 591 patients receiving cemiplimab including 1 (0.2%) patient with Grade 3 hyperthyroidism. No patient discontinued cemiplimab due to hyperthyroidism. Among the 11 patients with hyperthyroidism, the median time to onset was 1.9 months (range: 28 days to 14.8 months).

Adrenal insufficiency occurred in 3 (0.5%) of 591 patients receiving cemiplimab including 1 (0.2%) patient with Grade 3 adrenal insufficiency. No patient discontinued cemiplimab due to adrenal insufficiency. Among the 3 patients with adrenal insufficiency, the median time to onset was 11.5 months (range: 10.4 months to 12.3 months). One of the 3 patients was treated with systemic corticosteroids.

Hypophysitis occurred in 1 (0.2%) of 591 patients receiving cemiplimab. The event was Grade 3 hypophysitis.

Type 1 diabetes mellitus without an alternative aetiology occurred in 4 (0.7%) of 591 patients including 3 (0.5%) patients with Grade 4 and 1 (0.2%) patient with Grade 3 type 1 diabetes mellitus. Type 1 diabetes mellitus led to permanent discontinuation of cemiplimab in 1 (0.2%) of 591 patients. Among the 4 patients with type 1 diabetes mellitus, the median time to onset was 2.3 months (range: 28 days to 6.2 months).

Immune-related skin adverse reactions

Immune-related skin adverse reactions occurred in 12 (2.0%) of 591 patients receiving cemiplimab including 6 (1.0%) patients with Grade 3 immune-related skin adverse reactions. Immune-related skin adverse reactions led to permanent discontinuation of cemiplimab in 2 (0.3%) of 591 patients. Among the 12 patients with immune-related skin adverse reactions, the median time to onset was 1.5 months (range: 2 days to 10.9 months) and the median duration was 4.4 months (range: 14 days to 9.6 months). Nine patients (1.5%) with immune-related skin adverse reactions received high-dose corticosteroids for a median of 16 days (range: 7 days to 2.6 months). Resolution had occurred in 6 (50%) of 12 patients at the time of data cut-off.

Immune-related nephritis

Immune-related nephritis occurred in 3 (0.5%) of 591 patients receiving cemiplimab including 2 (0.3%) patients with Grade 3 immune-related nephritis. Immune-related nephritis led to permanent discontinuation of cemiplimab in 1 (0.2%) of 591 patients. Among the 3 patients with immune-related nephritis, the median time to onset was 1.8 months (range: 29 days to 4.1 months) and the median duration of nephritis was 18 days (range: 9 days to 29 days). Two (0.3%) patients with immune-related nephritis received high-dose corticosteroids for a median of 1.5 months (range: 16 days to 2.6 months). Resolution of nephritis had occurred in all patients at the time of data cut-off.

Other immune-related adverse reactions

The following clinically significant, immune-related adverse reactions occurred at an incidence of less than 1% of 591 (unless otherwise specified) patients treated with cemiplimab. The events were Grade 3 or less unless stated otherwise:

Nervous system disorders: Meningitis[a] (Grade 4), paraneoplastic encephalomyelitis (Grade 5), Guillain-Barre syndrome, central nervous system inflammation, chronic inflammatory demyelinating polyradiculoneuropathy, encephalitis[b], myasthenia gravis, neuropathy peripheral[c].

Cardiac Disorders: Myocarditis[d], pericarditis[e]

Immune system disorders: Immune thrombocytopenic purpura

Vascular disorders: Vasculitis

Musculoskeletal and connective tissue disorders: Arthralgia (1.4%), arthritis[f], muscular weakness, myalgia, polymyalgia rheumatica, Sjogren's syndrome

Eye disorders: Keratitis

Gastrointestinal disorders: Stomatitis

Endocrine: Thyroiditis

[a] includes meningitis and meningitis aseptic
[b] includes encephalitis and noninfective encephalitis
[c] includes neuritis and neuropathy peripheral
[d] includes autoimmune myocarditis and myocarditis
[e] includes autoimmune pericarditis and pericarditis
[f] includes arthritis and polyarthritis

Infusion-related reactions

Infusion-related reactions occurred in 54 (9.1%) of 591 patients treated with cemiplimab including 1 (0.2%) patient with Grade 3 infusion-related reaction. Infusion-related reaction led to permanent discontinuation of cemiplimab in 2 (0.3%) patients. The most common symptoms of infusion-related reaction were nausea, pyrexia, vomiting, abdominal pain, chills and flushing. All patients recovered from the infusion-related reaction.

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity with cemiplimab. Five out of 398 patients (1.3%) administered cemiplimab developed treatment-emergent antibodies, with 1 out of 398 patients (0.3%) exhibiting persistent antibody responses. No neutralizing antibodies have been observed. There was no evidence of an altered PK or safety profile with anti-cemiplimab antibody development.

Postmarketing Experience

The following adverse reactions have been reported during post-approval use of LIBTAYO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure (see Section 4.4).

Blood and lymphatic system disorders: HLH

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions at https://nzphvc.otago.ac.nz/reporting/.

4.9 OVERDOSE

In case of overdose, patients should be closely monitored for signs or symptoms of adverse reactions, and appropriate symptomatic treatment instituted.

For advice on the management of overdose, please contact the New Zealand National Poisons Information Centre (telephone 0800 POISON or 0800 764 766)

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

This medicine has been given a provisional consent under Section 23 of the Act. This means that further evidence on this medicine is awaited or that there are specific conditions of use. The decision to approve this indication has been made on the basis of objective response rate (ORR) and duration of response from single arm clinical studies. Refer to the consent notice published in the New Zealand Gazette for the specific conditions.

Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies. ATC code: L01XC33.

Mechanism of action

Cemiplimab is a fully human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with its ligands PD-L1 and PD-L2. Engagement of PD-1 with its ligands PD-L1 and PD-L2, which are expressed by antigen presenting cells and may be expressed by tumour cells and/or other cells in the tumour microenvironment, results in inhibition of T cell function such as proliferation, cytokine secretion, and cytotoxic activity. Cemiplimab potentiates T cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands.

Clinical efficacy and safety

The efficacy and safety of cemiplimab in patients with mCSCC (nodal or distant) or laCSCC who were not candidates for curative surgery or curative radiation were studied in clinical trial R2810-ONC-1540 (Study 1540). Study 1540 was a phase 2, open label, multi-centre study that enrolled 193 patients with mCSCC or laCSCC with a combined median duration of follow up time of 9.4 months total. Median duration of follow up was 16.5 months for the mCSCC 3 mg/kg every 2 weeks (Q2W) group, 9.3 months for the laCSCC 3 mg/kg Q2W group and 8.1 months for the mCSCC 350 mg every 3 weeks (Q3W) group.

Patients with any of the following were excluded: autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years; history of solid organ transplant; history of pneumonitis within the last 5 years; prior treatment with anti PD-1/PD-L1 or other immune checkpoint inhibitor therapy; active infection requiring therapy, including known infection with human immunodeficiency virus, or active infection with hepatitis B or hepatitis C virus; chronic lymphocytic leukaemia (CLL); brain metastases or Eastern Cooperative Oncology Group (ECOG) performance score (PS) ≥2.

In Study 1540, patients received cemiplimab until progression of disease, unacceptable toxicity or completion of planned treatment [3 mg/kg Q2W for 96 weeks or 350 mg Q3W for 54 weeks]. If patients with locally advanced disease showed sufficient response to treatment, surgery with curative intent was permitted. Tumour response assessments were performed every 8 or 9 weeks (for patients receiving 3 mg/kg Q2W or 350 mg Q3W, respectively). The primary endpoint of Study 1540 was confirmed objective response rate (ORR), as assessed by independent central review (ICR). For patients with mCSCC without externally visible target lesions, ORR was determined by Response Evaluation Criteria in Solid Tumours (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). The key secondary endpoint was duration of response (DOR) by ICR. Other secondary endpoints included ORR and DOR by investigator assessment (IA), progression free survival (PFS) by ICR and IA, overall survival (OS), complete response rate (CR) by ICR, and change in scores in patient reported outcomes on the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (EORTC QLQ-C30).

Results are presented from 193 patients in Study 1540. Of these 193 patients, 115 had mCSCC and 78 had laCSCC. The median age was 72 years (range: 38 to 96): Seventy-eight (40.4%) patients were 75 years or older, 66 patients (34.2%) were 65 to less than 75 years, and 49 patients (25.4%) were less than 65 years. A total of 161 (83.4%) patients were male, and 187 (96.9%) patients were White; the ECOG PS was 0 (44.6%) and 1 (55.4%). Thirty-three and 7/10 per cent (33.7%) of patients had received at least 1 prior anti-cancer systemic therapy, 90.2% of patients had received prior cancer related surgery, and 67.9% of patients had received prior radiotherapy. Among patients with mCSCC, 76.5% had distant metastases, and 22.6% had only nodal metastases.

Efficacy results for Study 1540 are presented in Table 3.

Table 3 - Efficacy results: Study 1540 - metastatic CSCC by dosing group, locally advanced CSCC

	mCSCC cemiplimab: 3 mg/kg Q2W (Group 1) (N = 59)	**laCSCC cemiplimab: 3 mg/kg Q2W (Group 2) (N = 78)**	**mCSCC cemiplimab: 350 mg Q3W (Group 3) (N = 56)**
	ICR	ICR	ICR
Confirmed objective response rate (ORR) [a]			
ORR	49.2%	43.6%	41.1%

	mCSCC cemiplimab: 3 mg/kg Q2W (Group 1) (N = 59)	laCSCC cemiplimab: 3 mg/kg Q2W (Group 2) (N = 78)	mCSCC cemiplimab: 350 mg Q3W (Group 3) (N = 56)
	ICR	ICR	ICR
95% CI for ORR	(35.9, 62.5)	(32.4, 55.3)	(28.1, 55.0)
Complete response (CR) [b]	16.9%	12.8%	5.4%
Partial response (PR)	32.2%	30.8%	35.7%
Stable disease (SD)	15.3%	35.9%	14.3%
Progressive disease (PD)	16.9%	11.5%	25.0%
Duration of response (DOR)			
Median[c] (months)	NR	NR	NR
Range (months)	(2.8-21.6+)	(1.9 – 24.2+)	(2.1-11.1+)
Patients with DOR ≥ 6 months	93.1%	67.6%	65.2%
Time to response			
Median (months) range (min:max)	1.9 (1.7: 9.1)	1.9 (1.8: 8.8)	2.1 (2.0: 8.3)
Progression free survival (PFS) [a, c]			
6 months (95% CI)	65.8% (51.8, 76.7)	71.5% (58.9, 80.9)	59.3% (45.0, 71.0)
12 months (95% CI)	52.9% (39.0, 65.0)	58.1% (43.7, 70.0)	47.4% (29.6, 63.3)
Overall survival [a, c]			
12 months (95% CI)	81.3% (68.7, 89.2)	93.2% (84.4, 97.1)	76.1% (56.9, 87.6)

Data cut-off was Sep 20, 2018 for Groups 1 and 3 patients, and Oct 10, 2018 for Group 2 patients.

CI: confidence interval; ICR: Independent Central Review; NR: Not Reached; +: Denotes ongoing at last assessment; Q2W: every 2 weeks; Q3W: every 3 weeks

a. In Groups 1, 2, and 3, median durations of follow-up were 16.5, 9.3, and 8.1 months, respectively.
b. Only includes patients with complete healing of prior cutaneous involvement; laCSCC patients in Study 1540 required biopsy to confirm complete response.
c. Based on Kaplan Meier estimates

Efficacy and PD-L1 status

Clinical activity was observed regardless of tumour PD-L1 expression status. The relationship between PD-L1 status and efficacy was analysed post-hoc in patients with available tissue samples. Overall in Studies 1423 and 1540, PD-L1 IHC results were

available for 75 advanced CSCC patients. Among 22 advanced CSCC patients with PD-L1 <1%, ORR per ICR was 40.9% (9/22). Among 53 advanced CSCC patients with PD-L1 ≥1%, ORR was 54.7% (29/53). Among 21 mCSCC patients, ORR was 60% (3/5) in patients with PD-L1 <1% and 56.3% (9/16) among patients with PD-L1 ≥1%. Among 54 patients with laCSCC, ORR was 35.3% (6/17) in patients with PD-L1 <1% and 54.1% (20/37) among patients with PD-L1 ≥1%.

Elderly population

Of the 219 patients with mCSCC and laCSCC treated with cemiplimab, 25.1% (55/219) were less than 65 years, 34.2% (75/219) were 65 to less than 75 years, and 40.6% (89/219) were 75 years or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

In the 193 patients in the efficacy analysis, the ORR by ICR (95% CI) was 40.8% (27.0%, 55.8%) in patients less than 65 years, 48.5% (36.0%, 61.1%) in patients 65 to less than 75 years, and 43.6% (32.4%, 55.3%) in patients 75 years or older.

5.2 PHARMACOKINETIC PROPERTIES

Concentration data were collected in 548 patients with various solid tumours, including 178 patients with CSCC, who received cemiplimab. At dosing regimens of 1 mg/kg to 10 mg/kg Q2W and 350 mg Q3W, kinetics of cemiplimab were observed to be linear and dose proportional, suggesting saturation of the target-mediated pathway over the dosing interval.

Similar exposures to cemiplimab are achieved with the doses of 350 mg every 3 weeks (Q3W) and 3 mg/kg every 2 weeks. Population-predicted mean steady state concentrations of cemiplimab (N=548) at 350 mg Q3W ranged between a C_{trough} of 61 mg/l and a C_{max} of 168 mg/l. In patients with mCSCC receiving 350 mg Q3W (N=53), observed mean cemiplimab concentrations at steady-state ranged between a C_{trough} of 63 mg/l and a concentration at end of infusion (C_{max}) of 151 mg/l. Steady state exposure is achieved after approximately 4 months of treatment.

Absorption

Cemiplimab is administered via the intravenous route and hence is completely bioavailable.

Distribution

Cemiplimab is primarily distributed in the vascular system with a volume of distribution at steady state (VSS) of 5.2 litres.

Metabolism

Specific metabolism studies were not conducted because cemiplimab is a protein. Cemiplimab is expected to degrade to small peptides and individual amino acids.

Elimination

Clearance of cemiplimab is linear at doses of 1 mg/kg to 10 mg/kg every two weeks. Cemiplimab clearance after the first dose is approximately 0.33 l/day. The total clearance appears to decrease by approximately 35% over time, resulting in a steady state clearance (CL_{ss}) of 0.21 l/day; the decrease in CL is not considered clinically relevant. The within dosing interval half-life at steady state is 19.4 days.

Linearity/non-linearity

At the dosing regimens of 1 mg/kg to 10 mg/kg every two weeks, kinetics of cemiplimab were observed to be linear and dose proportional, suggesting saturation of the target-mediated pathway.

Special populations

A population PK analysis suggests that the following factors have no clinically significant effect on the exposure of cemiplimab: age, gender, body weight, race, cancer type, albumin level, mild hepatic impairment and renal impairment.

Renal impairment

The effect of renal impairment on the exposure of cemiplimab was evaluated by a population PK analysis in patients with mild (CL_{cr} 60 to 89 mL/min; n= 197), moderate (CL_{cr} 30 to 59 mL/min; n= 90), or severe (CL_{cr} 15 to 29 mL/min; n= 4) renal impairment. No clinically important differences in the exposure of cemiplimab were found between patients with renal impairment and patients with normal renal function. Cemiplimab has not been studied in patients with CL_{cr} <25 mL/min (see Section 4.2).

Hepatic impairment

The effect of hepatic impairment on the exposure of cemiplimab was evaluated by population PK analysis. In patients with mild hepatic impairment (n=5) (total bilirubin greater than 1.0 to 1.5 times the upper limit of normal [ULN] and any aspartate aminotransferase [AST]); no clinically important differences in the exposure of cemiplimab were found compared to patients with normal hepatic function. Cemiplimab has not been studied in patients with moderate or severe hepatic impairment. There are insufficient data in patients with moderate or severe hepatic impairment for dosing recommendations (see Section 4.2).

5.3 PRECLINICAL SAFETY DATA

No studies have been performed to test the potential of cemiplimab for carcinogenicity or genotoxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Histidine

Histidine monohydrochloride monohydrate

Sucrose

Proline

Polysorbate 80

Water for injections

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products except those mentioned in Section 6.6.

6.3 SHELF LIFE

Unopened vial

30 months

After opening

Once opened, the medicinal product should be diluted and infused immediately (see Section 6.6 for instructions on dilution of the medicinal product before administration).

After preparation of infusion

Libtayo does not contain a preservative.

Once prepared, to reduce microbiological hazard administer the diluted solution immediately. If diluted solution is not administered immediately, it may be stored temporarily either:

- at room temperature up to 25°C for no more than 8 hours from the time of infusion preparation to the end of infusion.

  Or

- under refrigeration at 2°C to 8°C for no more than 24 hours from the time of infusion preparation to the end of infusion. Do not freeze. Allow the diluted solution to come to room temperature prior to administration.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Unopened vial

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Store in the original carton in order to protect from light.

For storage conditions after first opening or dilution of the medicinal product, see Section 6.3.

6.5 NATURE AND CONTENTS OF CONTAINER

LIBTAYO is provided in a 10 mL clear Type 1 glass vial, with a grey chlorobutyl stopper with FluroTec coating and seal cap with a flip-off button.

Each carton contains 1 vial.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Preparation and administration

- Visually inspect medicinal product for particulate matter and discoloration prior to administration. LIBTAYO is a clear to slightly opalescent, colourless to pale yellow solution that may contain trace amounts of translucent to white particles
- Discard the vial if the solution is cloudy, discoloured or contains extraneous particulate matter other than a few translucent to white particles.
- Do not shake the vial.
- Withdraw 7 mL (350 mg) from the vial of LIBTAYO and transfer into an intravenous infusion bag containing sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection. Mix the diluted solution by gentle inversion. Do not shake the solution. The final concentration of the diluted solution should be between 1 mg/mL to 20 mg/mL.
- LIBTAYO is administered by intravenous infusion over 30 minutes through an intravenous line containing a sterile, non-pyrogenic, low-protein binding, in-line or add-on filter (0.2 micron to 5 micron pore size).
- Do not co-administer other medicinal products through the same infusion line.

LIBTAYO is for single use only. In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

7 MEDICINE SCHEDULE

Prescription

8 SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644

Toll Free Number (medical information): 0800 283 684

Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

29 June 2023

10 DATE OF REVISION

14 August 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2, 4.4, 4.8	Safety update to add information relating to Haemophagocytic lymphohistiocytosis (HLH)
8	Update to Sponsor details