ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Cejemly 600 mg concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial of 20 mL of concentrate for solution for infusion contains 600 mg of sugemalimab.

Each mL of concentrate contains 30 mg of sugemalimab.

Sugemalimab is a fully human anti-programmed death-ligand 1 (PD-L1) monoclonal antibody (IgG4 isotype) produced in Chinese hamster ovary cells by recombinant DNA technology.

Excipient with known effect

One vial contains 25.8 mg of sodium.
This medicine contains 2.04 mg of polysorbate 80 in each vial.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.

Clear to opalescent, colourless to slight yellow solution, essentially free from visible particles, pH 5.3 to 5.7.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cejemly in combination with platinum-based chemotherapy is indicated for the first-line treatment of adults with metastatic non-small-cell lung cancer (NSCLC) with no sensitising EGFR mutations, or ALK, ROS1 or RET genomic tumour aberrations.

Cejemly as monotherapy is indicated for the treatment of unresectable stage III NSCLC with no sensitising EGFR mutations, or ALK, ROS1 genomic tumour aberrations in adults whose tumours express PD-L1 on ≥ 1% of tumour cells and whose disease has not progressed following platinum-based chemoradiotherapy.

4.2 Posology and method of administration

Therapy should be initiated and supervised by physicians experienced in the use of anticancer medicinal products.

PD-L1 testing for patients with unresectable stage III NSCLC
To determine eligibility for treatment, tumour cell PD-L1 expression should be assessed with a CE-marked IVD with the corresponding intended purpose. If a CE-marked IVD is not available, an alternative validated test should be used.

Posology

The use of systemic corticosteroids or immunosuppressants before starting sugemalimab should be avoided (see section 4.5).

Recommended dose

The recommended dose of Cejemly monotherapy and Cejemly combination therapy is presented in Table 1. Cejemly is administered as an intravenous infusion over 60 minutes.

When Cejemly is administered in combination with chemotherapy, refer to the Summary of Product Characteristics (SmPC) of the combination products (see also section 5.1).

Table 1: Recommended dose for Cejemly by intravenous administration

Indication	Recommended dose and schedule	Duration of Treatment
Cejemly monotherapy		
Unresectable Stage III NSCLC consolidation treatment	• 1200 mg (for individuals weighing 115 kg or less) every 3 weeks or • 1500 mg (for individuals weighing more than 115 kg) every 3 weeks	Treatment should be continued until disease progression, or unacceptable toxicity.
Cejemly combination therapy		
First line squamous metastatic NSCLC	During platinum-based chemotherapy: • 1200 mg (for individuals weighing 115 kg or less) followed by intravenous infusion of carboplatin and paclitaxel on day 1 for up to 4 cycles every 3 weeks; • 1500 mg (for individuals weighing more than 115 kg) followed by intravenous infusion of carboplatin and paclitaxel on day 1 for up to 4 cycles every 3 weeks. Post-platinum-based chemotherapy: • 1200 mg (for individuals weighing 115 kg or less) every 3 weeks for the duration of the therapy; • 1500 mg (for individuals weighing more than 115 kg) every 3 weeks for the duration of the therapy.	Treatment should be continued until disease progression, or unacceptable toxicity.
First line non-squamous metastatic NSCLC	During platinum-based chemotherapy: • 1200 mg (for individuals weighing 115 kg or less) followed by intravenous infusion of carboplatin and pemetrexed on day 1 for up to 4 cycles every 3 weeks; • 1500 mg (for individuals weighing more than 115 kg) followed by intravenous infusion of carboplatin and pemetrexed on day 1 for up to 4 cycles every 3 weeks. Post-platinum-based chemotherapy: • 1200 mg (for individuals weighing 115 kg or less) and pemetrexed are administered every 3 weeks for the duration of the therapy; • 1500 mg (for individuals weighing more than 115 kg) and pemetrexed are administered every 3 weeks for the duration of the therapy.	Treatment should be continued until disease progression, or unacceptable toxicity.

Treatment modification

The dose of sugemalimab should not be increased or reduced. Treatment withholding or discontinuation may be required based on individual safety and tolerability. Recommended treatment modifications are provided in Table 2.

Table 2. Recommended treatment modifications of Cejemly

Adverse reaction	Severity*	Treatment modification
Immune-related pneumonitis	Grade 2	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 3 or 4, or recurrent Grade 2	Permanently discontinue.
Immune-related colitis	Grade 2 or 3	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 4 or recurrent Grade 3	Permanently discontinue.
Immune-related nephritis	Grade 2 blood creatinine increased	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 3 or 4 blood creatinine increased	Permanently discontinue.
Immune-related pancreatitis	Grade 2 pancreatitis†	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 3 or 4 pancreatitis	Permanently discontinue.
Immune-related ocular toxicities	Grade 2 ocular toxicities	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 3 or 4 ocular toxicities	Permanently discontinue.
Immune-related endocrine disorders	Symptomatic Grade 2 or 3 hypothyroidism Grade 2 or 3 hyperthyroidism Grade 2 or 3 symptomatic hypophysitis Grade 2 adrenal insufficiency Type-1 diabetes mellitus associated Grade 3 hyperglycaemia	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 4 hypothyroidism Grade 4 hyperthyroidism Grade 4 symptomatic hypophysitis Grade 3 or 4 adrenal insufficiency Type-1 diabetes mellitus associated Grade 4 hyperglycaemia	Permanently discontinue.
Immune-related hepatitis	Grade 2, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) at > 3 to 5 times the upper limit of normal (ULN) or total bilirubin (TBIL) at > 1.5 to 3 times the ULN	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 3 or 4, AST or ALT > 5 times the ULN, or TBIL > 3 times the ULN	Permanently discontinue.
Immune-related skin reactions	Grade 3 Suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Withhold until the adverse reaction recovers to Grade 0 to 1.

Adverse reaction	Severity*	Treatment modification
	Grade 4 Confirmed SJS or TEN	Permanently discontinue.
Other immune-related adverse reactions	First occurrence of other Grade 2 or Grade 3 immune-related adverse reactions depending on the reaction severity and type	Withhold until the adverse reaction recovers to Grade 0 to 1.
	Grade 2, 3 or 4 myocarditis Grade 3 or 4 encephalitis Grade 4 myositis First occurrence of other Grade 4 immune-related adverse reactions	Permanently discontinue.
Recurrent immune-related adverse reactions	Recurrent Grade 3 or 4 (except for endocrine disorders)	Permanently discontinue.
Infusion-related reactions	Grade 2	Infusion should be interrupted and may be resumed at 50% of previous rate once infusion related reactions have resolved or decreased to Grade ≤1, with close observation ensured.
	Grade 3 or 4	Permanently discontinue.
Non-immune-mediated adverse reactions	Grade 2 and 3	Withhold until non-immune-mediated adverse reactions recovers to Grade 0 to 1.
	Grade 4	Permanently discontinue.

***** Toxicity Grades are in accordance with the National Cancer Institute's Common Terminology Criteria for Adverse Events, Version 4.03 (NCI CTCAE V4.03).

† Continued clinical monitoring is recommended for asymptomatic pancreatitis or increase in pancreatic enzyme / lipase, but no temporary medicinal products discontinuation is required.

Special populations

Elderly

No treatment modification of sugemalimab is required for elderly patients (≥ 65 years of age) (see section 5.1).

Renal impairment

No treatment modification of sugemalimab is required in patients with mild or moderate renal impairment (see section 5.2). Sugemalimab has not been studied in patients with severe renal impairment. Sugemalimab must be administered with caution in patients with severe renal impairments.

Hepatic impairment

No treatment modification of sugemalimab is recommended for patients with mild hepatic impairment (see section 5.2). Sugemalimab has not been studied in patients with moderate or severe hepatic impairment. Sugemalimab must be administered with caution in patients with moderate or severe hepatic impairment.

Paediatric population

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

Method of administration
Cejemly is for intravenous use only.

Sugemalimab after dilution is administered as an intravenous infusion over 60 minutes.

Sugemalimab must not be administered as an intravenous push or bolus injection. For the management of infusion-related reactions, see Table 2.

The diluted sugemalimab solution is administered first, followed by chemotherapy. Chemotherapy may be started 30 minutes after completion of sugemalimab administration.

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
Immune-related adverse reactions, including serious and fatal cases, have occurred in patients receiving sugemalimab. Immune-related adverse reactions can occur after discontinuation of treatment. In clinical studies, most immune-related adverse reactions were reversible and managed with interruptions of sugemalimab treatment, administration of corticosteroids and/or supportive care. Immune-related adverse reactions affecting more than one body system can occur simultaneously.

For suspected immune-related adverse reactions, ensure adequate evaluation to confirm aetiology or exclude other causes. Based on the severity of the adverse reaction, withhold, or permanently discontinue sugemalimab and consider administration of corticosteroids. Upon improvement to Grade 1 or 0, initiate corticosteroid taper and continue to taper for at least 1 month. Restart sugemalimab if the adverse reaction remains at Grade 1 or 0 following corticosteroid tapering. If another episode of the severe adverse reaction occurs, permanently discontinue sugemalimab (see sections 4.2 and 4.4).

Immune-related pneumonitis
Immune-related pneumonitis has been reported in patients receiving sugemalimab (see section 4.8). Patients should be monitored for signs and symptoms of pneumonitis. Suspected pneumonitis should be confirmed with radiographic imaging to exclude other causes. For Grade 2 pneumonitis, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg /day prednisone or equivalent should be administered. If symptoms improve to Grade 0 or 1, corticosteroids should be tapered for at least 1 month. Treatment with sugemalimab may be resumed if the event remains at Grade 0 to 1 following corticosteroid tapering. Sugemalimab should be permanently discontinued for severe (Grade 3), life-threatening (Grade 4) or recurrent moderate (Grade 2) pneumonitis (see section 4.2) and 1 to 2 mg/kg /day of methylprednisolone or equivalent should be administered.

Pneumonitis and Radiation pneumonitis
Radiation pneumonitis is frequently observed in patients receiving radiation therapy to the lung and the clinical presentation of pneumonitis and radiation pneumonitis is very similar.
In the Study GEMSTONE-301, in patients who had completed treatment with at least 2 cycles concurrent or sequential chemoradiation within 1 to 42 days prior to initiation of study treatment, pneumonitis or radiation pneumonitis have been reported.

Patients should be monitored for signs and symptoms of pneumonitis or radiation pneumonitis. Suspected radiation pneumonitis should be confirmed with radiographic imaging and other infectious and disease-related aetiologies excluded and managed as recommended in section 4.2.

Immune-related skin reactions
Immune-related severe skin reactions have been reported in patients receiving sugemalimab (see section 4.8). Patients should be monitored for suspected severe skin reactions and other causes should be excluded. For Grade 3 skin reactions, sugemalimab should be withheld until recovery to Grade 0 to 1 and 1 to 2 mg/kg/day of prednisone or equivalent should be administered. Sugemalimab should be permanently discontinued for Grade 4 skin reactions, and corticosteroids should be administered.

Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in patients receiving PD-1/PD-L1 immune checkpoint inhibitors. For suspected SJS or TEN, sugemalimab should be withheld and the patient should be referred to a specialised unit for assessment and treatment. For confirmed SJS or TEN, sugemalimab should be permanently discontinued (see section 4.2).

Caution should be used when considering the use of sugemalimab in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anti-cancer agents.

Immune-related colitis
Immune-related colitis has been reported in patients receiving sugemalimab monotherapy (see section 4.8). Patients should be monitored for signs and symptoms of colitis and other causes should be excluded. For Grade 2 colitis, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg/day prednisone or equivalent should be administered. For Grade 3 colitis, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg/day methylprednisolone or equivalent should be administered. Treatment with sugemalimab may be resumed if the event remains at Grade 0 to 1 following corticosteroid tapering. Sugemalimab should be permanently discontinued for life-threatening (Grade 4) or recurrent Grade 3 colitis (see section 4.2), and 1 to 2 mg/kg/day methylprednisolone or equivalent should be administered.

Immune-related hepatitis
Immune-related hepatitis has occurred in patients receiving sugemalimab (see section 4.8). Patients should be monitored for abnormal liver tests prior to and as clinically indicated during treatment with sugemalimab. For Grade 2 hepatitis, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg/day prednisone or equivalent should be administered. Treatment with sugemalimab may be resumed if the event remains at Grade 0 or 1 following corticosteroid tapering. Sugemalimab should be permanently discontinued for severe (Grade 3) or life-threatening (Grade 4) hepatitis (see section 4.2), and 1 to 2 mg/kg/day methylprednisolone or equivalent should be administered.

Immune-related nephritis
Immune-related nephritis has been reported in patients receiving sugemalimab (see section 4.8). Patients should be monitored for abnormal renal function tests prior to and periodically during treatment with sugemalimab and managed as recommended. For Grade 2 nephritis, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg/day prednisone or equivalent should be administered. For Grade 2 nephritis, treatment with sugemalimab may be resumed if the event remains at Grade 0 to 1 following corticosteroid tapering. Sugemalimab should be permanently discontinued for severe (Grade 3) or life-threatening (Grade 4) nephritis (see section 4.2) and 1 to 2 mg/kg/day methylprednisolone or equivalent should be administered.

Immune-related endocrinopathies
Immune-related endocrinopathies including hyperthyroidism, hypothyroidism, thyroiditis, diabetes mellitus, adrenal insufficiency and hypophysitis have been reported in patients receiving sugemalimab treatment (see section 4.8).

Thyroid disorders have been reported in patients receiving sugemalimab, including hyperthyroidism, hypothyroidism and thyroiditis. These can occur at any time during treatment; therefore, patients should be monitored for changes in thyroid function and clinical signs and symptoms of thyroid disorders (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation).

For symptomatic hypothyroidism, sugemalimab should be withheld and thyroxine replacement therapy should be initiated as needed. For symptomatic hyperthyroidism sugemalimab should be withheld and an anti-thyroid medication should be initiated as needed. Treatment with sugemalimab may be resumed when symptoms are controlled, and thyroid function is improving. Sugemalimab should be permanently discontinued for life-threatening (Grade 4) hypothyroidism and hyperthyroidism (see section 4.2).

Type-1 diabetes mellitus has been reported in patients receiving sugemalimab. Patients should be monitored for hyperglycaemia or other signs and symptoms of diabetes and managed with insulin as clinically indicated. For type-1 diabetes mellitus associated with Grade 3 hyperglycaemia sugemalimab should be withheld. Treatment with sugemalimab may be resumed if metabolic control is achieved on insulin replacement therapy. Sugemalimab should be permanently discontinued for type-1 diabetes mellitus associated with life-threatening (Grade 4) hyperglycaemia (see section 4.2).

Adrenal insufficiency has been reported in patients receiving sugemalimab. Hypophysitis has also been reported in patients receiving sugemalimab. Patients should be monitored for signs and symptoms of adrenal insufficiency or hypophysitis (including hypopituitarism) and other causes should be excluded. For Grade 2 adrenal insufficiency or for Grade 2 or 3 hypophysitis, treatment with sugemalimab should be withheld (see section 4.2), and treatment with sugemalimab may be resumed if the event improves to Grade 0 to 1. Corticosteroids to treat adrenal insufficiency or hypophysitis and other hormone replacement therapy (such as thyroxine in patients with hypophystitis) should be administered as clinically indicated. Pituitary function and hormone levels should be monitored to ensure appropriate hormone replacement. Sugemalimab should be permanently discontinued for Grade 3 or 4 adrenal insufficiency and for Grade 4 hypophysitis.

Immune-related myositis
Immune-related myositis has been reported in patients receiving sugemalimab at very low frequency or with delayed onset of symptoms (see section 4.8). Patients should be monitored for potential myositis and other causes should be excluded. If a patient develops signs and symptoms of myositis, close monitoring should be implemented, and the patient referred to a specialist for assessment and treatment without delay. Based on the severity of the adverse reaction, withhold, or permanently discontinue sugemalimab (see section 4.2). For Grade 2 myositis, 1 to 2 mg/kg/day prednisone or equivalent should be administered. For Grade 3 or 4 myositis, methylprednisolone 1 to 2 mg/kg/day or equivalents should be administered.

Immune-related myocarditis
Immune-related myocarditis has been reported in patients receiving sugemalimab (see section 4.8). Monitor patients for suspected myocarditis and exclude other causes. If myocarditis is suspected, treatment with sugemalimab should be withheld, prompt initiation of systemic corticosteroids at a dose of 1 to 2 mg/kg/day of prednisone or equivalent should be started, and prompt cardiology consultation with diagnostic workup according to current clinical guidelines should be initiated. Once a diagnosis of myocarditis is established, sugemalimab should be permanently discontinued for Grade 2, 3 or 4 myocarditis (see section 4.2).

Immune-related pancreatitis
Immune-related pancreatitis has been reported in patients receiving sugemalimab (see section 4.8). Patients should be closely monitored for signs of symptoms suggestive of acute pancreatitis and for increases in serum amylase or lipase. For Grade 2 pancreatitis, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg/day prednisone or equivalent should be administered. For Grade 2 pancreatitis, treatment with sugemalimab may be resumed if the event remains at Grade 0 to 1 following corticosteroid tapering. Sugemalimab should be permanently discontinued for severe

(Grade 3) or life-threatening (Grade 4) pancreatitis (see section 4.2) and 1 to 2 mg/kg/day methylprednisolone or equivalent should be administered.

Immune-related ocular toxicities
Immune-related ocular toxicities have been reported in patients receiving sugemalimab (see section 4.8). For Grade 2 ocular toxicities, treatment with sugemalimab should be withheld, and 1 to 2 mg/kg/day prednisone or equivalent should be administered. For Grade 2 ocular toxicities, treatment with sugemalimab may be resumed if the event remains at Grade 0 to 1 following corticosteroid tapering. Sugemalimab should be permanently discontinued for severe (Grade 3) or life-threatening (Grade 4) ocular toxicities (see section 4.2) and 1 to 2 mg/kg/day methylprednisolone or equivalent should be administered.

Other immune-related adverse reactions
Other immune-related adverse reactions including immune-related upper gastrointestinal disorders, immune-related arthritis, immune-related pancytopenia/bicytopenia, immune-related meningoencephalitis/encephalitis, immune-related Guillain-Barre syndrome/demyelination, immune-related rhabdomyolysis/myopathy,immune-related hemolytic anemia, and immune-related vasculitis were reported in patients receiving sugemalimab (see section 4.8).

Patients should be monitored for suspected immune-related adverse reactions, adequate evaluation should be performed to confirm aetiology or exclude other causes. Based on the severity of the adverse reaction, withhold, or permanently discontinue sugemalimab (see section 4.2). For Grade 2 immune-mediated adverse reactions, 1 to 2 mg/kg/day prednisone or equivalent should be administered. For Grade 3 or 4 adverse reactions, methylprednisolone 1 to 2 mg/kg/day or equivalents should be administered.

Infusion -related reactions
Infusion-related reactions including anaphylactic reaction, hyperhidrosis, pyrexia, chills, erythema and rash, have been reported in patients receiving sugemalimab (see section 4.8). Patients should be closely monitored for clinical signs and symptoms of an infusion reaction and managed as recommended in section 4.2.

Patients excluded from clinical studies
Patients with the following conditions were excluded from clinical study: active autoimmune disease; receiving immunosuppressive treatment; live-virus vaccine administration within 28 days of the study treatment start; HIV infection, hepatitis B or hepatitis C infection; a history of interstitial lung disease or idiopathic pulmonary fibrosis.

Sodium
This medicinal product contains 51.6 mg sodium per 1200 mg dose and 64.5 mg sodium per 1500 mg dose, equivalent to 2.58% and 3.23% of the WHO recommended maximum daily intake of 2 grams for an adult. However, sodium chloride 9 mg/mL (0.9%) solution for infusion is used for the dilution of Cejemly prior to administration and this should be taken into consideration in the context of the daily sodium intake of the patient.

Polysorbate 80
This medicine contains 4.08 mg of polysorbate 80 in each 1200 mg dose and 5.10 mg polysorbate 80 in each 1500 mg dose. Polysorbates may cause allergic reactions.

Patient card
All physicians administering sugemalimab must be familiar with the Physician Information and Management Guidelines. The physician must discuss the risks of sugemalimab therapy with the patient. The patient will be provided with the patient card and instructed by the physician to carry the card at all times.

4.5 Interaction with other medicinal products and other forms of interaction

No formal pharmacokinetic (PK) interaction studies have been conducted with sugemalimab. Since sugemalimab is cleared from the circulation through catabolism, no metabolic interactions with other medicinal products are expected.

The use of systemic corticosteroids or immunosuppressants before starting sugemalimab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of sugemalimab. However, systemic corticosteroids or other immunosuppressants can be used after starting sugemalimab to treat immune -related adverse reactions (see section 4.4).

4.6 Fertility, pregnancy, and lactation

Women of childbearing potential/Contraception in females
Women of childbearing potential must be advised to avoid pregnancy during treatment with sugemalimab. Women of childbearing potential receiving sugemalimab should use reliable contraception methods during treatment and for at least 4 months after the last dose of sugemalimab (see below and section 5.3).

Pregnancy
There are no data on the use of sugemalimab in pregnant women. Animal reproduction and developmental toxicity studies have not been conducted with sugemalimab. However, blockade of PD-L1 signalling in murine models of pregnancy has been shown to disrupt tolerance to the foetus and to increase foetal loss (see section 5.3).

Sugemalimab is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding
It is unknown whether sugemalimab is secreted in human milk. Since it is known that antibodies can be secreted in human milk, a risk to the newborns/infants cannot be excluded. A decision should be made whether to discontinue breast-feeding or to discontinue sugemalimab treatment, taking into account the benefit of breast-feeding for the child and the benefit of sugemalimab therapy for the woman.

Fertility
No clinical data are available on the possible effects of sugemalimab on fertility. Animal data did not show notable effects on the male and female reproductive organs (see section 5.3).

4.7 Effects on ability to drive and use machines

Sugemalimab has minor influence on the ability to drive and use machines. In some patients, fatigue has been reported following administration of sugemalimab (see section 4.8). Patients experiencing fatigue should be advised not to drive and use machines until the symptoms resolved.

4.8 Undesirable effects

Summary of the safety profile
The safety of sugemalimab has been evaluated in 1003 patients receiving 1200 mg every 3 weeks in clinical studies across tumour types. 435 out of those 1003 patients received sugemalimab in combination with chemotherapy, and 568 out of those 1003 patients received sugemalimab as monotherapy.

The incidence of adverse reactions in patients treated in combination with chemotherapy was 95.6%. The most common adverse reactions (≥10%) were anaemia (77.5%), hepatic enzyme increased (42.5%), rash (26.2%), hyperlipidaemia (21.6%), hyperglycaemia (18.4%), hyponatraemia (16.8%), hypokalaemia (15.6%), hypothyroidism (15.6%), hyperthyroidism (15.2%), proteinuria (14.0%),

abdominal pain (13.8%), fatigue (13.3%), arthralgia (12.2%), hypoaesthesia (11.5%) and hypocalcaemia (10.1%). The incidence of Grade ≥ 3 adverse reactions in these patients was 33.1%. The most common Grade ≥ 3 adverse reactions (> 1%) were anaemia (17.5%), hyponatraemia (4.4%), hypokalaemia (3.0%), hyperlipidaemia (2.3%), hepatic enzyme increased (2.3%), amylase increased (2.1%), hepatic function abnormal (1.8%), hyperglycaemia (1.6%), fatigue (1.4%), rash (1.4%), hypertension (1.4%) and pneumonitis (1.1%).

The incidence of adverse reactions in patient treated with monotherapy was 81.5%. The most common adverse reactions (≥ 10%) were hepatic enzyme increased (28.3%), anaemia (22.9%), hypothyroidism (22.5%), rash (17.1%), pyrexia (15.3%), hyperthyroidism (14.4%), blood bilirubin increased (13.0%), hyperlipidaemia (12.9%), proteinuria (12.3%) and hyperglycaemia (10.9%). The incidence of Grade ≥ 3 adverse reactions in these patients was 16.7%. The most common Grade ≥ 3 adverse reactions (> 1%) were anaemia (3.2%), hepatic enzyme increased (3.0%), blood bilirubin increased (1.8%), hypertension (1.6%), hypokalaemia (1.4%), hyponatraemia (1.4%), rash (1.2%) and hyperlipidaemia (1.2%).

Tabulated list of adverse reactions

Adverse drug reactions observed in clinical studies of sugemalimab in combination with chemotherapy and sugemalimab as monotherapy are listed in Table 3. These reactions are presented 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) and very rare (< 1/10 000). Within each frequency grouping, adverse reactions are presented in the order of decreasing frequency.

Table 3. Adverse reactions

	In combination with chemotherapy	**Monotherapy**
Blood and lymphatic system disorders		
Very common	anaemia	anaemia
Uncommon	immune-related pancytopenia/bicytopenia*	haemolytic anaemia
Immune system disorders		
Uncommon	anaphylactic reaction	hypersensitivity, anti-neutrophil cytoplasmic antibody positive vasculitis
Endocrine disorders		
Very common	hypothyroidism[a,#],hyperthyroidism[b,#]	hypothyroidism[a,#], hyperthyroidism[b,#]
Uncommon	immune-related hypophysitis*, adrenal insufficiency, immune-mediated thyroiditis	immune-related hypophysitis*
Metabolism and nutrition disorders		
Very common	hyperlipidaemia[c], hyperglycaemia[d], hyponatraemia, hypokalaemia, hypocalcaemia[e]	hyperlipidaemia[c], hyperglycaemia[d]
Common	hyperuricaemia[f], hypochloraemia[g], hypomagnesaemia, diabetes mellitus[#]	hypokalaemia, hyponatraemia
Uncommon	dyslipidaemia	diabetes mellitus[#]

Nervous system disorders		
Very common	hypoaesthesia[h]	
Common	neuropathy peripheral	
Uncommon	immune-mediated encephalitis, immune-related Guillain-Barre syndrome/demyelination*	
Eye disorders		
Common	conjunctivitis, dry eye	
Uncommon		conjunctivitis
Cardiac disorders		
Common	tachycardia[i]	tachycardia[i]
Uncommon	immune-mediated myocarditis	myocarditis[j]
Vascular disorders		
Common	hypertension	hypertension
Respiratory, thoracic, and mediastinal disorders		
Common	pneumonitis[k]	pneumonitis[k]
Gastrointestinal disorders		
Very common	abdominal pain[l]	
Common	stomatitis[m], dry mouth	diarrhoea, stomatitis[m]
Uncommon	pancreatitis, proctitis	colitis[#]
Hepatobiliary disorders		
Very common	hepatic enzyme increased[n]	hepatic enzyme increased[n], blood bilirubin increased[o]
Common	hepatic function abnormal, blood bilirubin increased[o], hepatitis[p]	hepatic function abnormal
Uncommon		hepatitis[p]
Skin and subcutaneous tissue disorders		
Very common	rash[q]	rash[q]
Common	skin hypopigmentation[r]	
Musculoskeletal and connective tissue disorders		
Very common	arthralgia	
Common	myalgia, bone pain	arthralgia, myalgia
Uncommon	immune-mediated arthritis	myositis[s], immune-mediated arthritis
Renal and urinary disorders		
Very common	proteinuria[t]	proteinuria[t]
Common	blood creatinine increased, nephritis[u,#]	blood creatinine increased, nephritis[u,#]
General disorders and administration site conditions		
Very common	fatigue	pyrexia
Common		fatigue

Investigations		
Common	blood creatine phosphokinase increased[v], amylase increased, lipase increased	blood creatine phosphokinase increased[v], amylase increased
Uncommon	troponin T increased, cortisol decreased	troponin T increased,
Injury, poisoning and procedural complications		
Common	infusion related reaction	
Uncommon		infusion related reaction

*Grouped terms which refer to a class effect of immune-related adverse reaction. In clinical studies of sugemalimab in monotherapy or combination with chemotherapy, only myelosuppression, blood corticotrophin decreased, and neuritis were observed respectively under immune-related pancytopenia/bicytopenia, hypophysitis, and Guillain-Barre syndrome/demyelination.
The ADR can be immune-related adverse reaction.

The following terms represent a group of related events that describe a medical condition rather than a single event:

a. Hypothyroidism (hypothyroidism, blood thyroid stimulating hormone increased, thyroxine free decreased, tri-iodothyronine free decreased)
b. Hyperthyroidism (hyperthyroidism, blood thyroid stimulating hormone decreased, thyroxine increased, thyroxine free increased, tri-iodothyronine free increased)
c. Hyperlipidaemia (hyperlipidaemia, hypercholesterolaemia, hypertriglyceridaemia, blood triglycerides increased, blood cholesterol increased)
d. Hyperglycaemia (hyperglycaemia, blood glucose increased)
e. Hypocalcaemia (hypocalcaemia, blood calcium decreased)
f. Hyperuricaemia (hyperuricaemia, blood uric acid increased)
g. Hypochloraemia (hypochloraemia, blood chloride decreased)
h. Hypoaesthesia (hypoaesthesia, anaesthesia)
i. Tachycardia (tachycardia, sinus tachycardia, supraventricular tachycardia, atrial tachycardia, atrial fibrillation, ventricular fibrillation)
j. Myocarditis (myocarditis, immune-mediated myocarditis)
k. Pneumonitis (pneumonitis, immune-mediated lung disease, interstitial lung disease)
l. Abdominal pain (abdominal pain, abdominal discomfort, abdominal distension, abdominal pain upper)
m. Stomatitis (stomatitis, mouth ulceration)
n. Hepatic enzyme increased (alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, gamma-glutamyltransferase increased, transaminases increased)
o. Blood bilirubin increased (blood bilirubin unconjugated increased, bilirubin conjugated increased, blood bilirubin increased)
p. Hepatitis (hepatitis, immune-mediated hepatic disorder, immune-mediated hepatitis, drug-induced liver injury, hepatic failure)
q. Rash (rash, rash maculo-papular, eczema, erythema, dermatitis, dermatitis acneiform, rash erythematous, rash pruritic, urticaria, pruritus, immune-mediated dermatitis, papule, drug eruption)
r. Skin hypopigmentation (skin hypopigmentation, skin depigmentation, leukoderma)
s. Myositis (myositis, immune-mediated myositis)
t. Proteinuria (proteinuria, protein urine present)
u. Nephritis (nephritis, renal impairment, renal injury, renal failure, acute kidney injury)
v. Blood creatine phosphokinase increased (blood creatine phosphokinase increased, blood creatine phosphokinase MB increased)

Description of selected adverse reactions

Data for the following immune-related adverse reactions are based on information from 1003 patients, of whom 435 patients were treated with sugemalimab in combination with chemotherapy and 568 patients were treated with sugemalimab monotherapy in clinical studies. The management guidelines for these adverse reactions are described in section 4.4.

Immune-related adverse reactions

Immune-related hypothyroidism
Immune-related hypothyroidism was reported in 14.3% of patients treated with sugemalimab in combination with chemotherapy. The majority of events were Grade 1 or 2 in severity reported in 9.2% and 4.8% of patients, respectively. Grade 3 hypothyroidism was reported in 0.2% of patients. No serious hypothyroidism was reported. Events led to treatment interruption and discontinuation were reported in 0.9% and 0.2% of patients, respectively. The median time to onset was 112 days (range: 16 to 607 days), and the median duration was 83 days (range: 1^+ to 857^+ days).
Immune-related hypothyroidism was reported in 16.7% of patients treated with sugemalimab monotherapy. The majority of events were Grade 1 or 2 in severity reported in 10.9% and 5.1% of patients, respectively. Grade 3 hypothyroidism was reported in 0.7% of patients. No serious hypothyroidism was reported. Events led to treatment interruption and discontinuation were reported in 1.6% and 0.2% of patients, respectively. The median time to onset was 92 days (range: 20 to 683 days), and the median duration was 125 days (range: 2^+ to 979^+ days).

Immune-related hyperthyroidism
Immune-related hyperthyroidism was reported in 9.4% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity reported in 8.7% and 0.7% of patients, respectively. There were no serious events, or events led to treatment interruption or discontinuation. The median time to onset was 91 days (range: 20 to 620 days), and the median duration was 44 days (range: 10 to 484^+ days).
Immune-related hyperthyroidism was reported in 11.3% of patients treated with sugemalimab monotherapy. The majority of events were Grade 1 or 2 in severity reported in 9.0% and 2.1% of patients, respectively. Grade 3 hyperthyroidism was reported in 0.2% of patients. There were no serious events, or events led to treatment discontinuation. Events led to treatment interruption were reported in 0.4% of patients. The median time to onset was 44.5 days (range: 20 to 692 days), and the median duration was 43 days (range: 9 to 1000^+ days).

Immune-related thyroiditis
Immune-related thyroiditis was reported in 0.5% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 in severity. There were no serious events, or events led to treatment interruption or discontinuation. The median time to onset was 136 days (range: 105 to 167 days), and the median duration was not reached (range: 736^+ to 835^+ days).
Immune-related thyroiditis was reported in 0.5% of patients treated with sugemalimab monotherapy. All events were Grade 1 and 2 in severity reported in 0.4% and 0.2% of patients, respectively. There were no serious events, or events led to treatment discontinuation. Events led to treatment interruption were reported in 0.2% of patients. The median time to onset was 42 days (range: 40 to 104 days), and the median duration was 122.5 days (range: 22 to 616^+ days).

Diabetes mellitus
Immune-related diabetes mellitus was reported in 2.8% of patients treated with sugemalimab in combination with chemotherapy. The majority of events were Grade 1 in severity reported in 2.3% of patients. Grade 2 and Grade 3 events were reported in 0.2% of patients, respectively. There were no serious events, or events led to treatment interruption or discontinuation. The median time to onset was 154 days (range: 43 to 635 days), and the median duration was 41 days (range: 2 to 307^+ days).
Immune-related diabetes mellitus was reported in 2.3% of patients treated with sugemalimab monotherapy. The majority of events were Grade 1 and 2 in severity reported in 1.8 % and 0.4% of patients, respectively. Grade 3 events were reported in 0.2% of patients. There were no serious events, or events led to treatment interruption or discontinuation. The median time to onset was 101 days (range: 20 to 454 days), and the median duration was 43 days (range: 1 to 911^+ days).

Immune-related hypophysitis
Immune-related hypophysitis was reported in 0.9% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 in severity. There were no serious events, or events leading to treatment interruption or discontinuation. The median time to onset was 240.5 days (range: 112 to 754 days), and the median duration was not reached (range: 13^+ to 478^+ days).

Immune-related hypophysitis was reported in 0.4% of patients treated with sugemalimab monotherapy. All events were Grade 1 in severity. There were no serious events, or events leading to treatment interruption or discontinuation. The median time to onset was 168 days (range: 42 to 294 days), and the median duration was 22 days (range: 22 to 22 days).

Immune-related adrenal insufficiency
Immune-related adrenal insufficiency was reported in 0.2% of patients treated with sugemalimab in combination with chemotherapy. The event occurred in a single patient, was Grade 1 in severity, and did not lead to treatment interruption nor discontinuation.

Immune-related adrenal insufficiency was reported in 0.2% of patients treated with sugemalimab monotherapy. The event occurred in a single patient, was Grade 1 in severity, and did not lead to treatment interruption nor discontinuation.

Immune-related skin adverse reactions
Immune-related skin adverse reactions (excluding severe) were reported in 10.6% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity and were reported in 7.1% and 3.4% of patients, respectively. Immune-related skin adverse reaction (excluding severe) leading to treatment interruption were reported in 0.9% of patients. There were no serious events or events leading to treatment discontinuation. The median time to onset was 158 days (range: 3 to 990 days), and the median duration was 31 days (range: 1 to 950^{+} days).

Immune-related skin adverse reactions (excluding severe) were reported in 9.2% of patients treated with sugemalimab monotherapy. All events were Grade 1 and 2 in severity and were reported in 6.9% and 2.3% of patients, respectively. None of the events were serious or led to treatment interruption or discontinuation. The median time to onset was 53 days (range: 5 to 441 days), and the median duration was 77 days (range: 2 to 646^{+} days).

Immune-related severe skin adverse reaction was reported in 1.6% of patients treated with sugemalimab in combination with chemotherapy. Serious events were reported in 0.5% of patients, events leading to treatment interruption were reported in 0.9% of patients, and events leading to treatment discontinuation were reported in 0.5% of patients. The median time to onset was 312 days (range: 19 to 738 days), and the median duration was 95 days (range: 12 to 522^{+} days).

Immune-related severe skin adverse reaction was reported in 1.1% of patients treated with sugemalimab monotherapy. All events were Grade 3. None of the events were serious. Events leading to treatment interruption were reported in 0.7% of patients, and events leading to treatment discontinuation were reported in 0.2% of patients. The median time to onset was 13 days (range: 3 to 138 days), and the median duration was 285 days (range: 41 to 342^{+} days).

Immune-related hepatitis
Immune-related hepatitis was reported in 9.7% of patients treated with sugemalimab in combination with chemotherapy. Grade 1, 2, 3 and 4 events were reported in 5.7%, 1.4%, 2.3% and 0.2% of patients, respectively. Serious events were reported in 2.5% of patients. Events leading to treatment interruption and discontinuation were reported in 2.3% and 1.6% of patients, respectively. The median time to onset was 53 days (range: 1 to 717 days), and the median duration was 25 days (range: 2 to 777^{+} days).

Immune-related hepatitis was reported in 8.1% of patients treated with sugemalimab monotherapy.Grade 3,4 and 5 events were reported in 0.7%, 0.2%, and 0.2% of patients. Serious events were reported in 0.7% of patients. Events leading to treatment interruption and discontinuation were reported in 0.9% and 0.4% of patients, respectively. The median time to onset was 86.5 days (range: 20 to 509 days), and the median duration was 31 days (range: 5 to 470^{+} days).

Immune-related pancreatitis
Immune-related pancreatitis was reported in 3.4% of patients treated with sugemalimab in combination with chemotherapy. Grade 1, 2, 3 and 4 events were reported in 1.6%, 0.7%, 0.9% and 0.2% of patients, respectively. Serious events were reported in 0.2% of patients. Events leading to treatment interruption were reported in 0.5% of patients. No events leading to treatment discontinuation were reported. The median time to onset was 42 days (range: 20 to 629 days), and the median duration was 53 days (range: 2 to 958^{+} days).

Immune-related pancreatitis was reported in 1.2% of patients treated with sugemalimab monotherapy. The majority of events were Grade 1 or 2 in severity reported in 0.9% and 0.2% of patients, respectively. None of the events were serious or leading to treatment discontinuation. Events leading to dose interruption were reported in 0.2% of patients. The median time to onset was 42 days (range: 20 to 642 days), and the median duration was not reached (range: 22 to 979^{+} days).

Immune-related pneumonitis
Immune-related pneumonitis was reported in 3.0% of patients treated with sugemalimab in combination with chemotherapy. Grade 1, 2, 3 and 5 events were reported in 0.2%, 1.6%, 0.9% and 0.2% of patients, respectively. Serious events were reported in 2.1% of patients. Events led to treatment interruption and discontinuation were reported in 1.1% and 1.8% of patients, respectively. The median time to onset was 165 days (range: 6 to 903 days), and the median duration was 229 days (range: 18 to 558^{+} days).

Immune-related pneumonitis was reported in 9.3% of patients treated with sugemalimab monotherapy. Grade 1, 2, 3, 4 and 5 events were reported in 1.8%, 6.0%, 0.9%, 0.4% and 0.4% of patients, respectively. Serious events were reported in 4.8% of patients. Events leading to treatment interruption and discontinuation were reported in 4.0% and 3.0% of patients, respectively. The median time to onset was 63 days (range: 1 to 490 days), and the median duration was 556 days (range: 2 to 845^{+} days).

Immune-related pneumonitis occurred more frequently in patients in the Study GEMSTONE-301 who had completed treatment with concurrent or sequential chemoradiation within 1 to 42 days prior to initiation of study treatment (21.6%), than in the other patients in the monotherapy (1.3%).

In Study GEMSTONE-301 (n=255 in the sugemalimab group), immune- related pneumonitis occurred in 55 (21.6%) patients. Grade 1, 2, 3,4 and 5 events were reported in 3.1%, 14.9%, 2.4%, 0.8% and 0.4% of patients, respectively. Serious events were reported in 12.5% of patients. Events leading to treatment interruption and discontinuation were reported in 8.6% and 8.2% of patients, respectively. The median time to onset was 63 days (range: 1 to 784 days), and the median duration was not estimable (range: 9 to 1601 days).

Immune-related myositis
Immune-related myositis was reported in 2.5% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity and were reported in 0.9% and 1.6% of patients, respectively. Events led to treatment interruption were reported in 0.2% of patients. There were no serious events or events that led to treatment discontinuation. The median time to onset was 135 days (range: 3 to 649 days), and the median duration was 42 days (range: 2 to 655^{+} days).

Immune-related myositis was reported in 2.3% of patients treated with sugemalimab monotherapy. The majority of events were Grade 1 or 2 in severity reported in 1.2% and 0.9% of patients, respectively. Serious events were reported in 0.7% of patients. Events led to treatment interruption and discontinuation were reported in 0.2% and 0.5% of patients. The median time to onset was 64 days (range: 20 to 323 days), and the median duration was 71 days (range: 8 to 772^{+} days).

Immune-related colitis
Immune-related colitis was reported in 2.5% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity and were reported in 1.1% and 1.4% of patients, respectively. Events leading to treatment interruption were reported in 0.2% of patients. No

serious events or events leading to treatment discontinuation were reported. The median time to onset was 103 days (range: 1 to 682 days), and the median duration was 9 days (range: 2 to 445+ days).

Immune-related colitis was reported in 1.4% of patients treated with sugemalimab monotherapy. Grade 1 ,2 and 4 events were reported in 0.7%,0.5% and 0.2% of patients, respectively. Serious events were reported in 0.4% of patients. Events leading to treatment interruption were reported in 0.2% of patients. No events leading to treatment discontinuation were reported. The median time to onset was 43.5 days (range: 2 to 637 days), and the median duration was 11 days (range: 2 to 101+ days).

Immune-related myocarditis
Immune-related myocarditis was reported in 2.1% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity and were reported in 1.1% and 0.9% of patients, respectively. Serious events were reported in 0.7% of patients. Events leading to treatment interruption and discontinuation were reported in 1.1% and 0.2% of patients, respectively. The median time to onset was 221 days (range: 41 to 442 days), and the median duration was 23 days (range: 1 to 429+ days).

Immune-related myocarditis was reported in 2.8% of patients treated with sugemalimab monotherapy. All events were Grade 1 and 2 in severity and were reported in 2.1% and 0.7% of patients, respectively. Serious events were reported in 0.7% of patients. Events leading to treatment interruption and discontinuation were reported in 0.5% and 0.2% of patients, respectively. The median time to onset was 84 days (range: 21 to 505 days), and the median duration was not reached (range: 1 to 849+ days).

Immune-related nephritis
Immune-related nephritis (including renal failure) was reported in 1.8% of patients treated with sugemalimab in combination with chemotherapy. Grade 1, 2 and 3 events were reported in 0.9%, 0.2% and 0.7% of patients, respectively. Serious events were reported in 0.9% of patients. Events leading to treatment interruption and discontinuation were reported in 0.5% and 0.2% of patients, respectively. The median time to onset was 227.5 days (range: 26 to 539 days), and the median duration was 51.5 days (range: 5 to 543+ days).

Immune-related nephritis (including renal failure) was reported in 1.2% of patients treated with sugemalimab monotherapy. All events were Grade 1 or 2 patients in severity and were reported in 1.1% and 0.2% of patients, respectively. Events leading to dose interruption were reported in 0.2% of patients. None of the events were serious or led to treatment discontinuation. The median time to onset was 197 days (range: 42 to 446 days), and the median duration was 22 days (range: 6 to 570+ days).

Immune-related ocular toxicities
Immune-related ocular toxicities were reported in 1.4% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity and were reported in 0.7% and 0.7%, respectively. No serious events were reported. Events leading to treatment interruption and discontinuation were reported in 0.5% and 0.2% of patients, respectively. The median time to onset was 235.5 days (range: 137 to 482 days), and the median duration was 9.5 days (range: 1 to 181 days).

Immune-related ocular toxicities were reported in 0.2% of patients treated with sugemalimab monotherapy. The event occurred in a single patient, was Grade 2 in severity and led to treatment interruption.

Immune-related upper gastrointestinal disorders
Immune-related upper gastrointestinal disorder was reported in 0.9% of patients treated with sugemalimab in combination with chemotherapy. Grade 1, 2 and 3 events were reported in 0.5%, 0.2% and 0.2% of patients, respectively. Serious events were reported in 0.2% of patients. No events leading to treatment interruption or discontinuation were reported. The median time to onset was 146 days (range: 82 to 204 days), and the median duration was 385 days (range: 42 to 710 days).

Immune-related upper gastrointestinal disorder was reported in 0.5% of patients treated with sugemalimab monotherapy. All events were Grade 1 in severity. None of the events were serious or led to treatment interruption or discontinuation. The median time to onset was 5 days (range: 2 to 178 days), and the median duration was 8 days (range: 7 to 154 days).

Immune-related arthritis
Immune-related arthritis was reported in 0.9% of patients treated with sugemalimab in combination with chemotherapy. All events were Grade 1 and 2 in severity and were reported in 0.2% and 0.7% of patients, respectively. No serious events were reported. Events leading to treatment interruption were reported in 0.5% of patients. No events led to treatment discontinuation were reported. The median time to the onset was 173.5 days (range: 96 to 257 days), and the median duration was 98 days (range: 50 to 958^{+} days).

Immune-related arthritis was reported in 0.2% of patients treated with sugemalimab monotherapy. This event was occurred in a single patient, was of Grade 2 in severity. The event was not serious and did not lead to treatment interruption or discontinuation.

Immune-related pancytopenia/bicytopenia
Immune-related pancytopenia/bicytopenia was reported in 0.2% of patients treated with sugemalimab in combination with chemotherapy. The event occurred in a single patient, was Grade 4 in severity and serious, and did not lead to treatment interruption or discontinuation.

Immune-related pancytopenia/bicytopenia was reported in 0.4% of patients treated with monotherapy. All events were ≥ Grade 3 and serious. Events leading to treatment discontinuation were reported in 0.2% of patients. The median time to the onset of the first event was 109.5 days (range: 106 to 113 days), and the median duration was not reached (57+ to 239+ days).

Immune-related meningoencephalitis/encephalitis
Immune-related meningoencephalitis/encephalitis was reported in 0.2% of patients treated with sugemalimab in combination with chemotherapy. The event occurred in a single patient, was of Grade 2 in severity and led to treatment discontinuation.

No event of immune-related meningoencephalitis/encephalitis was reported in patients treated with sugemalimab monotherapy.

Immune-related Guillain-Barre syndrome/demyelination
Immune-related Guillain-Barre syndrome/demyelination was reported in 0.2% of patients treated with sugemalimab in combination with chemotherapy. The event occurred in a single patient, was of Grade 2 in severity and serious, and did not lead to treatment interruption or discontinuation.

No event of immune-related Guillain-Barre syndrome/demyelination was reported in patients treated with sugemalimab monotherapy.

Immune-related rhabdomyolysis/myopathy
Immune-related rhabdomyolysis/myopathy was reported in 0.2% of patients treated with sugemalimab in combination with chemotherapy. The event occurred in a single patient, was of with Grade 2 in severity and led to treatment interruption.

Immune-related rhabdomyolysis/myopathy was reported in 0.2% of patients treated with sugemalimab monotherapy. The event occurred in a single patient, was of Grade 1 in severity. The event was not serious and did not lead to treatment interruption or discontinuation.

Immune-related hemolytic anemia
No event of immune-related hemolytic anemia was report in patients treated with sugemalimab in combination with chemotherapy.

Immune-related hemolytic anemia was reported in 0.2% of patients treated with sugemalimab monotherapy. The event occurred in a single patient, was of Grade 4 in severity. The event was serious, and did not lead to treatment interruption or discontinuation.

Immune-related vasculitis
No event of immune-related vasculitis was report in patients treated with sugemalimab in combination with chemotherapy.

Immune-related vasculitis was reported in 0.2% of patients treated with sugemalimab monotherapy. The event occurred in a single patient, was of Grade 2 in severity. The event was serious and led to treatment discontinuation.

Immune checkpoint inhibitor class effects
There have been cases of the following adverse reaction(s) reported during treatment with other immune checkpoint inhibitors which might also occur during treatment with sugemalimab: pancreatic exocrine insufficiency, coeliac disease.

Infusion-related reactions
Infusion-related adverse reactions were reported in 4.4% of patients treated with sugemalimab in combination with chemotherapy. Reported events were infusion related reaction (0.9%), anaphylactic reaction (0.7%), hyperhidrosis (0.5%), pyrexia (0.5%), erythema, rash, rash maculo-papular, skin depigmentation, skin disorder, skin swelling, chills, oedema peripheral, tenderness, nausea, breath holding and throat irritation (0.2% each), respectively.

Infusion-related adverse reactions were reported in 3.3% of patients treated with sugemalimab monotherapy. Reported events were pyrexia (2.5%), infusion-related reaction (0.4%), and chills, pain, vomiting, dizziness, erythema, and pruritus (0.2% each), respectively.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No events of sugemalimab overdose have been reported in clinical studies. In case of overdose, patients must be closely monitored for signs or symptoms of adverse reactions, and appropriate symptomatic treatment should be initiated as dictated by patient's clinical status.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies and antibody drug conjugates, PD-1/PD-L1 (Programmed cell death protein 1/death ligand 1) inhibitors, ATC code: L01FF11.

Mechanism of action
Sugemalimab is a fully human immunoglobulin G4 monoclonal antibody. It specifically binds to programmed cell death ligand 1 (PD-L1), thus blocking its ligation with PD-1. PD-L1, when expressed on tumour cells and tumour-infiltrating immune cells, can contribute to the inhibition of an anti-tumour immune response. Binding of PD-L1 to the PD-1 and CD80 (B7.1) receptors found on T-cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation, and cytokine production. Blockade of PD-L1/PD-1 and PD-L1/CD80 interactions releases the inhibition of immune responses without inducing antibody dependent cell-mediated cytotoxicity (ADCC).

Clinical efficacy and safety

First-line treatment of metastatic NSCLC
GEMSTONE-302: *A randomized double-blind study of sugemalimab combined with platinum-based chemotherapy in first-line patients with advanced non-small cell lung cancer*

The efficacy and safety of sugemalimab in combination with platinum-based chemotherapy for the treatment of adults aged ≥ 18 years with histologically or cytologically confirmed metastatic (stage IV) squamous or non-squamous NSCLC without sensitising EGFR mutations, ALK fusions, ROS1, or RET translocations was studied in a randomised, double-blind, placebo-controlled phase 3 study (GEMSTONE-302). Apart from testing for EGFR mutational status in participants with non-squamous NSCLC, testing for genomic tumour aberrations/oncogenic drivers was not mandatory for enrolment. Participants had to provide formalin-fixed tumour tissue samples for PD-L1 assay. The PD-L1 expression was evaluated at a central laboratory by immunohistochemistry using the Ventana PD-L1 (SP263) assay on a BenchMark autostainer assay (Roche Tissue Diagnostics, Oro Valley, AZ, USA) according to the manufacturer's instructions. Participants were excluded if they had history of autoimmune disease, administration of systemic immunosuppressive medicinal product within 2 weeks prior to randomisation and active or untreated CNS metastases.

The primary endpoint of this study was progression-free survival (PFS) assessed by investigator according to RECIST v1.1. The secondary endpoints included overall survival (OS), PFS in participants with PD-L1 expression ≥ 1% (as assessed by investigators according to RECIST v1.1), objective response rate (ORR) assessed by investigators according to RECIST v1.1, and duration of response (DoR). The type I error was controlled using sequential testing method in the order of PFS, OS, PFS in participants with PD-L1 expression ≥ 1%, and ORR.

A total of 479 participants were randomly (2:1) assigned to receive:
- for squamous NSCLC, sugemalimab 1200 mg with carboplatin AUC = 5 mg/mL/min and paclitaxel 175 mg/m^2 intravenously administered every 3 weeks for up to 4 cycles, followed by sugemalimab 1200 mg-every 3 weeks
- for non-squamous NSCLC, sugemalimab 1200 mg with carboplatin AUC = 5 mg/mL/min and pemetrexed 500 mg/m^2 intravenously administered every 3 weeks for up to 4 cycles followed by sugemalimab 1200 mg and pemetrexed 500 mg/m^2 every 3 weeks

or
- placebo plus the same platinum-based chemotherapy regimens for squamous or non-squamous NSCLC as the group receiving sugemalimab for up to 4 cycles; then followed by placebo for squamous NSCLC, or placebo plus pemetrexed for non-squamous NSCLC.

The maximum duration of treatment with sugemalimab or placebo was 35 cycles (approximately 2 years) or until progressive disease, unacceptable toxicity, withdrawal of informed consent, death, or other reasons stipulated in the protocol.

Participants receiving placebo plus chemotherapy who experienced radiographic disease progression confirmed by investigator were able to cross-over to receive sugemalimab monotherapy.

During the first year of the treatment period, imaging assessments were performed at the 6th week and the 12th week after the first dose, and every 9 weeks thereafter; after 1 year: imaging assessments were

performed every 12 weeks until disease progression, loss to follow-up, death, or end of study, whichever occurred first.

All participants were Asian and had Stage IV NSCLC; the median age was 63.0 years; 80.0% were males; 73.3% were former or current smokers; 38.8% were ≥ 65 years; 40.1% had squamous NSCLC; 59.9% had non-squamous NSCLC; 60.8% had PD-L1 expression ≥ 1% of the tumour; 11.9% had liver metastases at baseline; 14.0% had brain metastases at baseline; 82.5% had an ECOG performance status of 1.

The median treatment duration was 10 cycles (range 1 to 49) with a median duration of 7.15 months for sugemalimab versus 6 cycles (range 1 to 44) with a median duration of 4.6 months for placebo. The efficacy results of the GEMSTONE-302 study are summarised in Table 4, Figure 1, and Figure 2.

Table 4. Efficacy results of the GEMSTONE-302 study

Efficacy endpoints	**Sugemalimab in combination with platinum-based chemotherapy** (n = 320)	**Placebo in combination with chemotherapy** (n = 159)
Progression free survival (PFS)*		
Number (%) participants with event	223 (69.7%)	135 (84.9%)
Median in months (95% CI)	9.0 (7.4, 10.8)	4.9 (4.8, 5.1)
Hazard ratio (95% CI)†	0.48 (0.39, 0.60)	
p-value†	< 0.0001	
Overall survival (OS)		
Number (%) participants with event	156 (48.8%)	97 (61.0%)
Median in months (95% CI)	25.4 (20.1, NR)	16.9 (12.8, 20.7)
Hazard ratio (95% CI)†	0.65 (0.50, 0.84)	
p-value†	0.0008	
Objective response rate*		
ORR n (%) (95% CI)	203 (63.4%) (57.9, 68.7)	64 (40.3%) (32.6, 48.3)
p-value§	< 0.0001	

CI = Confidence interval, ORR= Objective response rate

* Investigator assessed

† Hazard ratio (HR) is based on the stratified Cox model. P-value is based on the stratified log-rank test. The 3 stratification factors are ECOG performance status, PD-L1, and histology type from randomisation. See below for further explanation of histology type.

§ P value based on Cochran-Mantel-Haenszel test stratified by ECOG performance status, histology type and PD-L1 from randomisation.

Figure 1. Kaplan-Meier curve for investigator assessed progression-free survival – ITT population – study GEMSTONE-302

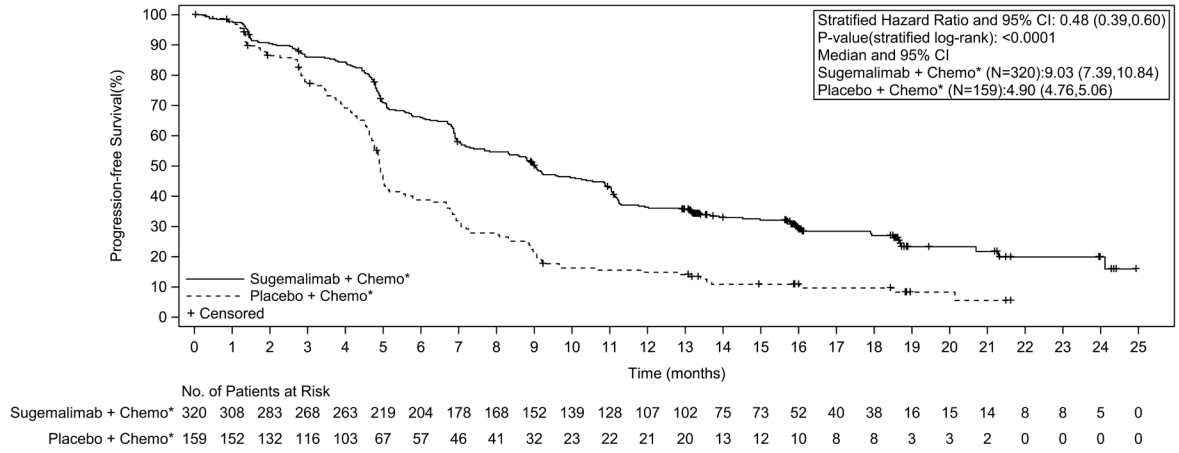


Figure 2. Kaplan-Meier curve of overall survival – ITT population – study GEMSTONE-302

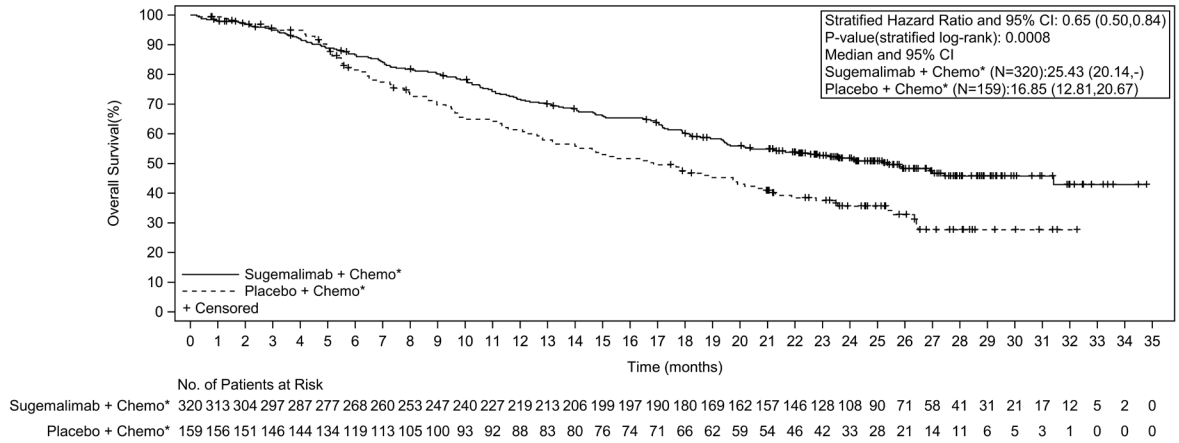
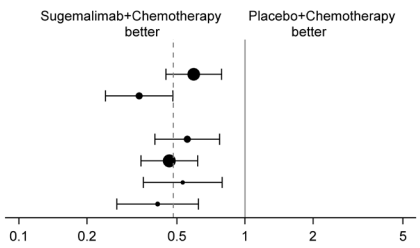


Figure 3. Forest-plot of PFS – study GEMSTONE-302

Baseline Risk Factor	Sugemalimab+ Chemotherapy (N=320) Event/n	Median	Placebo+ Chemotherapy (N=159) Event/n	Median	Hazard Ratio(95% CI)
Histology Type					
NSQ	128/191	9.56	78/96	5.85	0.59 (0.45, 0.79)
SQ	95/129	8.31	57/63	4.76	0.34 (0.24, 0.48)
PD-L1					
<1%	100/124	7.39	57/64	4.93	0.56 (0.40, 0.77)
>=1%	123/196	10.87	78/95	4.90	0.46 (0.35, 0.62)
>=1% and <50%	66/92	8.80	39/48	4.83	0.53 (0.35, 0.79)
>=50%	57/104	12.91	39/47	5.06	0.41 (0.27, 0.62)



Note: the subgroup analyses were not controlled for type 1 error.

Subgroup analysis showed improvements in PFS with sugemalimab, regardless of histological subtype and PD-L1, expression consistent with the overall intent-to-treat (ITT) population.

Consolidation treatment of unresectable stage III NSCLC

GEMSTONE-301: A randomized double-blind study of sugemalimab as consolidation therapy in patients with unresectable, stage III non-small cell lung cancer (NSCLC) who have not developed disease progression after receiving concurrent or sequential chemoradiotherapy

The efficacy and safety of sugemalimab as monotherapy for the treatment of adults aged ≥ 18 years with histologically or cytologically confirmed unresectable stage III NSCLC (staged according to the International Association for the Study of Lung Cancer [IASLC] classification, version 8) with no sensitising EGFR mutations, or ALK, ROS1 genomic tumour aberrations whose disease has not progressed after receiving concurrent or sequential chemoradiotherapy was studied in a randomised, double-blind, placebo-controlled phase 3 study (GEMSTONE-301). Apart from testing for EGFR mutational status in participants with non-squamous NSCLC, testing for genomic tumour aberrations/oncogenic drivers was not mandatory for enrolment. Test for PD-L1 status was not mandatory and was not systematically assessed. Participants had completed at least 2 cycles of definitive platinum-based chemotherapy with radiation therapy within 1 to 42 days prior to initiation of the study. Participants were excluded if they had history of autoimmune disease or administration of systemic immunosuppressive medicinal products (including systemic corticosteroid treatment equivalent to > 10 mg/day prednisone) within 1 week prior to randomisation.

The primary endpoint of this study was progression-free survival (PFS) assessed by a blinded independent central review committee (BICR) according to RECIST v1.1. Key secondary endpoint is overall survival (OS).

A total of 381 patients were randomly (2:1) assigned to groups to receive

- sugemalimab 1200 mg intravenously administered every 3 weeks

or

- placebo intravenously administered every 3 weeks

The maximum treatment duration with sugemalimab or placebo study drugs was two years or until progression of the disease or unacceptable toxicity.

During the first year of the treatment period, imaging assessments were performed every 9 weeks; after 1 year: imaging assessments were performed every 12 weeks until disease progression, loss to follow-up, death, or end of study, whichever occurred first.

All participants were Asian and 27.8% had stage IIIa NSCLC, 55.4% had stage IIIb NSCLC, and 16.0% had IIIc NSCLC; 92.1% were male, and median age was 61 years; 69.8% had squamous NSCLC, 29.7% had non-squamous NSCLC, 69.6% had an ECOG score of 1. 7.1% were current smoker, 77.7% were former smoker, 15.2% were never smoker. 66.7% received concurrent chemoradiotherapy before randomization, and 33.3% received sequential chemoradiotherapy. Of 175 participants with PD-L1 expression available, 54.3% were ≥ 1% and 45.7% were < 1%.

The median treatment duration was 12 cycles (range 1 to 72) with a median duration of 9.0 months for sugemalimab versus 10.0 cycles (range 1 to 60) with a median duration of 7.6 months for placebo.

The study demonstrated a statistically significant prolongation of PFS in the Sugemalimab group compared with the placebo group [hazard ratio (HR) = 0.65 (95% CI: 0.50, 0.84), p = 0.0012] at the final PFS analysis. The updated PFS results with longer follow-up and OS results of the GEMSTONE 301 are summarized in Table 5 and Figure 4. The median follow-up is 39.6 months.

Table 5. Efficacy Results for study GEMSTONE-301

Efficacy endpoints	**Sugemalimab** (n = 255)	**Placebo** (n = 126)
Progression free survival (PFS)		
Number (%) participants with event	169 (66.3%)	90 (71.4%)

Efficacy endpoints	Sugemalimab (n = 255)	Placebo (n = 126)
Median in months (95% CI)	10.6 (8.4, 16.8)	6.2 (4.2, 8.3)
Hazard ratio (95% CI)†	0.73 (0.56, 0.95)	
Overall survival (OS)		
Number (%) participants with event	114 (44.7%)	66 (52.4%)
Median in months (95% CI)	47.4 (34.3, NR)	32.4 (24.1, NR)
Hazard ratio (95% CI)†	0.78 (0.57, 1.05)	

CI = Confidence interval, NR=Not Reached

† Hazard ratio (HR) is based on the stratified Cox model. The 3 stratification factors are ECOG performance score, chemoradiotherapy and total radiotherapy dose.

Figure 4. Kaplan-Meier Curve of Progression-free Survival (PFS) Assessed by BICR – Intent-to-Treat Analysis Set – study GEMSTONE-301

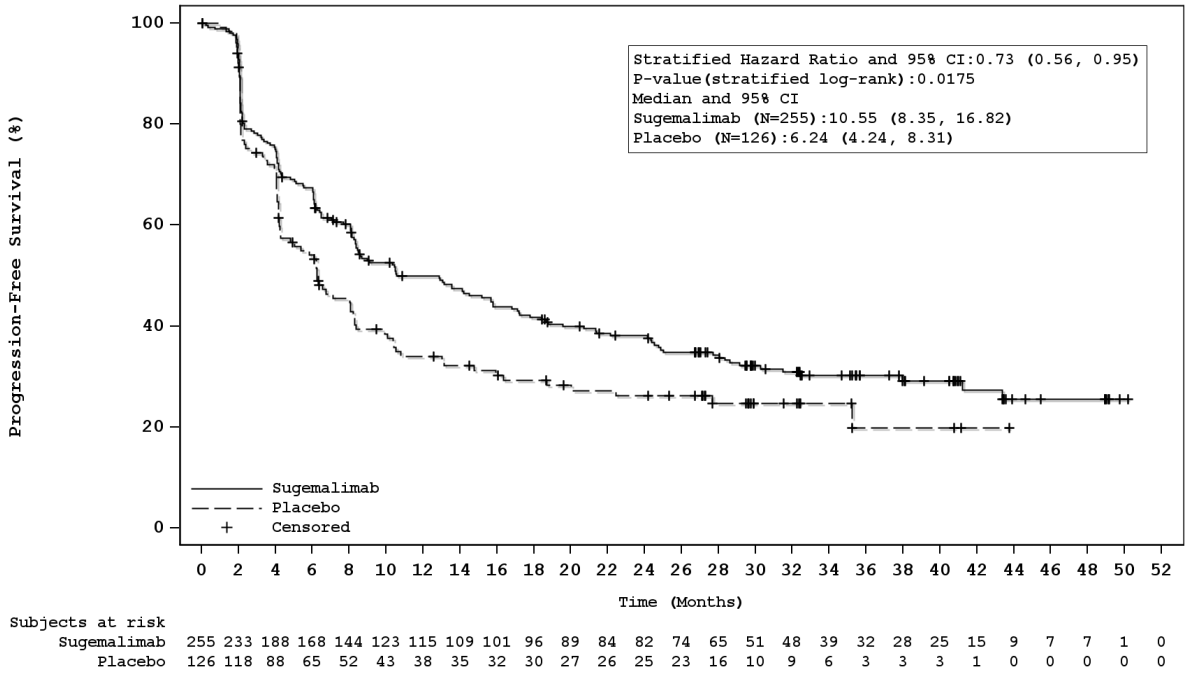
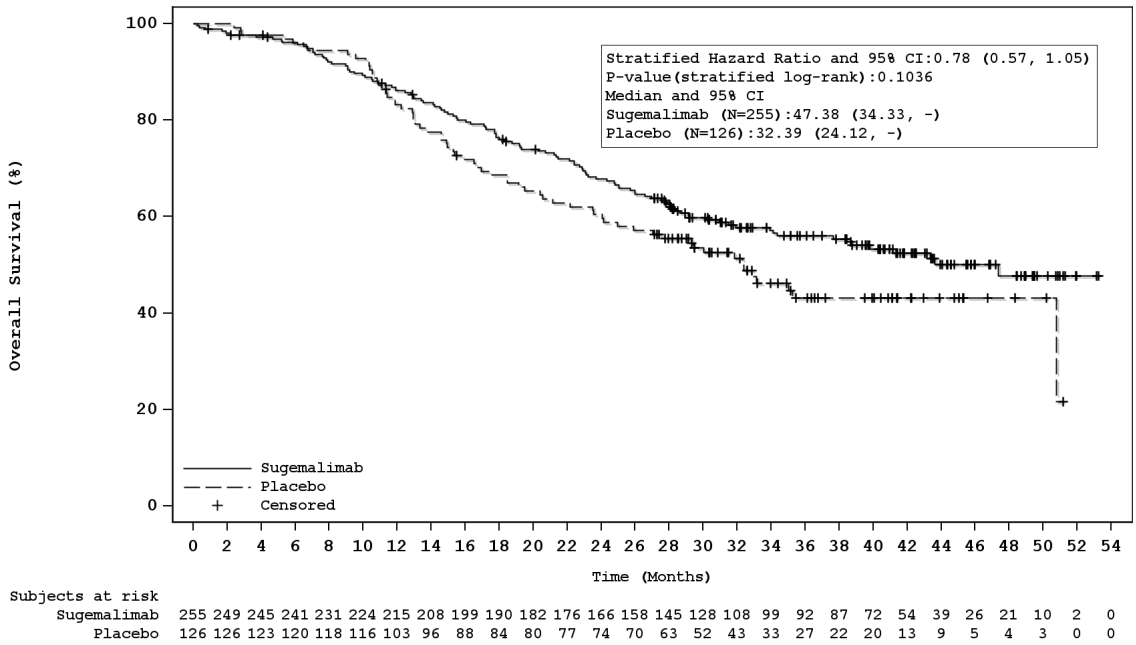


Figure 5. Kaplan-Meier Curve of Overall Survival (OS) – Intent-to-Treat Analysis Set – study GEMSTONE-301



Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with sugemalimab in the paediatric population in the treatment of lung cancer (see section 4.2 for information on paediatric use).

Immunogenicity
In the phase 3 stage IV NSCLC study (GEMSTONE-302), the prevalence of anti-drug antibodies (ADA) was 17% (53 patients), with 9% (28 patients) as treatment-emergent ADA.

In the phase 3 stage III NSCLC study (GEMSTONE-301), the prevalence of anti-drug antibodies (ADA) was 10.6% (27 patients), with 5.9% (15 patients) as treatment-emergent ADA.

No evidence was observed that ADA had an impact on pharmacokinetics, efficacy or safety, however data are still limited.

5.2 Pharmacokinetic properties

The PK of sugemalimab was characterised using population PK (PopPK) analysis with concentration data collected from 1002 participants who received sugemalimab doses in the range of 3 to 40 mg/kg and fixed dose of 1200 mg intravenous every 3 weeks.

Absorption
Sugemalimab is administered by intravenous infusion and therefore is immediately and completely bioavailable.

Following single- and multiple-doses escalation study of sugemalimab (n=29), sugemalimab exposures (AUC and C_{max}) increased in an approximately dose proportional manner within the dosing range of 3 mg/kg to 40 mg/kg, including a fixed dose of 1200 mg intravenous every 3 weeks. Following multiple intravenous infusions of 1200 mg every 3 weeks (n=16), there was approximately 2-fold accumulation of sugemalimab exposures (i.e., $R_{acc,Cmax}$ and $R_{acc,\ AUC}$ were 1.74 and 2.00, respectively).

Distribution
Consistent with a limited extravascular distribution of monoclonal antibodies, the volume of distribution of sugemalimab at steady-state (V_{ss}) from popPK analysis was small.

PopPK analysis estimated the geometric mean (CV%) Vss to be:
- 5.56 L (21%) in Stage IV NSCLC patients (Study GEMSTONE-302).
- 4.74 L (20%) in Stage III NSCLC patients (Study GEMSTONE-301).

Biotransformation
As an antibody, sugemalimab is catabolised through non-specific pathways; metabolism does not contribute to its clearance.

Elimination
In the PopPK analysis, geometric mean (CV%) of total clearance (CL) after a single dose was estimated to be 0.235 L/day (24.2%) in patients with stage IV NSCLC from Study GEMSTONE-302 and 0.214 L/day (23.8%) in patients with stage III NSCLC from Study GEMSTONE-301. At steady state, the elimination is slightly lower than after a single dose due to target-mediated drug disposition. Geometric mean (CV%) of the elimination half-life ($t_{1/2}$) estimated from the PopPK model was approximately 17.9 days (25.6%) at the end of cycle 1 in stage IV NSCLC patients (Study GEMSTONE-302) and 16.6 days (20.8%) at the end of cycle 1 in stage III NSCLC patients (Study GEMSTONE-301).

Special populations
Age, sex, body weight, tumour type, and anti-drug antibodies status
PopPK analysis showed non-statistically significant covariate effects of age (18-78 years) on sugemalimab exposure. The effect of other covariates (albumin, sex, anti-drug antibodies, and tumour type) on the systemic exposure of sugemalimab were not considered clinically meaningful. Based on the results from modelling and simulations, increasing the dosage to 1500 mg Q3W for NSCLC patients with body weight more than 115 kg, is anticipated to achieve comparable exposures to the patients in the pivotal studies that were dosed with 1200 mg Q3W.

Race
The effect of race in participants with advanced solid tumours (including NSCLC) receiving sugemalimab was evaluated by PopPK analysis and no impact of race was identified on the PK of sugemalimab. More specifically, there was no observed PK difference in sugemalimab between Asian and non-Asian participants.

Hepatic impairment
The effect of mild hepatic impairment on sugemalimab PK was evaluated using PopPK analyses. Covariate analysis indicated no statistically significant effect of markers of liver function (AST and ALT) on sugemalimab exposure.

Renal impairment
The effect of renal impairment on the clearance of sugemalimab was evaluated using PopPK analyses in participants with mild or moderate renal impairment compared to participants with normal renal function. There was no impact of renal function on PK of sugemalimab.

5.3 Preclinical safety data

No carcinogenicity or reproductive toxicity studies have been conducted with sugemalimab.

Based on literature assessment, the PD-L1/PD-1 signalling pathway plays a role in pregnancy by maintaining maternal immune tolerance to the foetus. In a mouse model of pregnancy, blocking PD-L1 signalling can destroy the immune tolerance to the foetus and increase foetal miscarriages. No foetal malformations associated with blocking PD-L1/PD-1 signalling pathway have been reported in the literature, but immune-related diseases have been observed in PD-1 and PD-L1 gene knockout

mice. Based on its mechanism of action, foetal exposure to sugemalimab may increase the risk of developing immune-related disorders or altering normal immune responses.

In 4- and 26-week repeat-dose toxicity studies in cynomolgus monkeys, exposure to sugemalimab administered IV once weekly, reveals no special hazard except two ophthalmic observations in high dose females: 1 incidence of retinal depigmentation and 1 case of medium-sized focal cornea opacity at 200 mg/kg, which corresponds to approximately 16-fold and 18-fold the clinical AUC at human recommended clinical dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Histidine
Histidine monohydrochloride
Mannitol (E421)
Sodium chloride
Polysorbate 80 (E433)
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

Unopened vial
36 months

Diluted medicinal product prepared for infusion
Chemical and physical in-use stability has been demonstrated for up to 24 hours at 2°C to 8°C and for up to 4 hours at room temperature (up to 25°C) from the time of preparation. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

20 mL of concentrate for solution for infusion in Type 1 glass vial with an elastomeric stopper and a blue flip-off aluminum seal containing 600 mg sugemalimab.

Pack size of 2 vials.

6.6 Special precautions for disposal and other handling

Cejemly is supplied as a single-use vial and does not contain any preservatives. Aseptic technique must be used for preparation and administration.

See SmPCs of platinum-based chemotherapy medicinal products and pemetrexed or paclitaxel for preparation.

Preparation and administration of Cejemly concentrate for solution for infusion

a. Do not shake the vial.

b. **1200 mg dose**
Withdraw 20 mL from each of the 2 vials (total 40 mL) of Cejemly using sterile syringe and transfer into a 250 ml intravenous bag containing sodium chloride 9 mg/mL (0.9%) solution for injection for a total 1200 mg dose. Mix diluted solution by gentle inversion. Do not freeze or shake the solution.
1500 mg dose
Withdraw 20 mL from each of 2 vials and 10 ml from 1 vial (total 50 mL) of Cejemly using sterile syringe and transfer into a 250 ml intravenous bag containing sodium chloride 9 mg/mL (0.9%) solution for injection for a total 1500 mg dose. Mix diluted solution by gentle inversion. Do not freeze or shake the solution.

c. Do not co-administer other medicinal products through the same infusion line. The infusion solution should be administered through an intravenous line containing a sterile, low-protein binding in-line or add-on polyether sulfone (PES) filter with a 0.22-micron pore size.

d. Allow the diluted solution to come to room temperature prior to administration.

e. Discard any unused portion left in the vial.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

CStone Pharmaceuticals Ireland Limited
117-126 Sheriff Street Upper
Dublin 1, D01 YC43
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1833/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 July 2024

10 DATE OF REVISION OF THE TEXT

<MM/YYYY>

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

WuXi Biologics Co., Ltd.
108 Meiliang Road
Mashan, Binhu District
Wuxi, Jiangsu 214092, China

Name and address of the manufacturer responsible for batch release

Manufacturing Packaging Farmaca (MPF) B.V.
Neptunus 12, 8448CN Heerenveen, Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c (7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimization measures**

The MAH shall ensure that in each Member State where Cejemly is marketed, all healthcare professionals and patients/carers who are expected to prescribe and use Cejemly have access to/are provided with the patient card.

The patient card shall contain the following key elements:

- Description of the main signs and symptoms of the irARs and the importance of notifying their treating physician immediately when symptoms occur.
- Reminder to carry the patient card at all times.
- Contact details of the Cejemly prescriber.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – 2 VIALS

1. NAME OF THE MEDICINAL PRODUCT

Cejemly 600 mg concentrate for solution for infusion
sugemalimab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 600 mg of sugemalimab in 20 ml (30 mg/ml).

3. LIST OF EXCIPIENTS

Excipients: histidine, histidine monohydrochloride, E421, sodium chloride, E433, water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Concentrate for solution for infusion
600 mg / 20 ml
2 vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use after dilution
For single-use only

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CStone Pharmaceuticals Ireland Limited
117-126 Sheriff Street Upper, Dublin 1, D01 YC43, Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1833/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT

Cejemly 600 mg concentrate for solution for infusion
sugemalimab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 600 mg of sugemalimab in 20 ml (30 mg/ml).

3. LIST OF EXCIPIENTS

Excipients: histidine, histidine monohydrochloride, E421, sodium chloride, E433, water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Concentrate for solution for infusion
600 mg / 20 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
IV use after dilution
For single-use only.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CStone Pharmaceuticals Ireland Limited

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1833/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Cejemly 600 mg concentrate for solution for infusion
Sugemalimab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- It is important that you keep the patient card with you during treatment.
- If you have any further questions, ask your doctor, or nurse.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cejemly is and what it is used for

What Cejemly is
Cejemly contains the active substance sugemalimab which is a monoclonal antibody (a type of protein) that attaches to a specific target in the body called PD-L1.

What Cejemly is used for
Cejemly is used to treat adults with a kind of lung cancer called ‘non-small cell lung cancer’. It is used alone when your lung cancer:
- has spread within your lung and cannot be removed by surgery, and has responded or stabilised after initial treatment with chemotherapy and radiotherapy.

It is used in combination with platinum-based chemotherapy when your lung cancer:
- has spread and cannot be removed by surgery

It is important that you read the package leaflets for the other anticancer medicines you may be receiving.

How Cejemly works
PD-L1 is found on the surface of certain tumour cells, and suppresses the body`s immune (defense) system, thereby protecting cancer cells from being attacked by the immune cells. Cejemly attaches to PD-L1 and helps your immune system to fight your cancer.

If you have any questions about how this medicine works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you are given Cejemly

Do not use Cejemly
You should not be given Cejemly if you are allergic to sugemalimab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or nurse before you are given Cejemly if:

- you have an autoimmune disease (a condition where the body attacks its own cells)
- you have been vaccinated with a live-virus vaccine in the 28 days before starting treatment
- you have a history of lung disease called radiation pneumonitis, interstitial lung disease or idiopathic pulmonary fibrosis
- you have or have had chronic viral infection of the liver, including hepatitis B (HBV) or hepatitis C(HCV)
- you have human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS)
- you have liver damage
- you have kidney damage

When you are given Cejemly, you can have some serious side effects. These side effects can sometimes become life-threatening and can lead to death. They may happen anytime during treatment or even weeks or months after your treatment has ended:

- Cejemly may cause infusion-related reactions (such as sudden severe swelling of face/throat/limb or anaphylaxis).
- Cejemly acts on your immune system and may cause inflammation in parts of your body. Inflammation may cause serious damage to your body and some inflammatory conditions may lead to death and need treatment or withdrawal of Cejemly. These reactions may involve one or more organ systems. This could result in inflammation and loss of function of the lungs, the stomach or intestines, the skin, the liver, the kidneys, the heart muscle, other muscles, or hormone glands.

For details, please see section 4 – Possible side effects. If you have any related symptoms, please contact the doctor immediately.

Children and adolescents
This medicine should not be given to patients under the age of 18 years as Cejemly has not been tested in children and adolescents.

Other medicines and Cejemly
Tell your doctor or nurse if you are taking, have recently taken or might take immunosuppressive treatment or any other medicines.
This includes medicines obtained without a prescription, including herbal medicines.

Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, you should not use this medicine. Talk with your doctor immediately if you become pregnant while you are being treated with Cejemly.

Contraception
If you are a female patient who can become pregnant, you must use reliable method of birth control to avoid becoming pregnant while being treated with Cejemly and for at least 4 months after the last dose.

Talk to your doctor about the reliable contraception methods that you must use during this time.

Breast-feeding
If you are breast-feeding or plan to breast-feed, you and the doctor will decide if you should use the product or breastfeed, you cannot do both.

Driving and using machines
Cejemly may have an influence on your ability to drive and use machines. If you feel tired, do not drive or use machines.

Cejemly contains sodium
This medicine contains 51.6 mg sodium per 1200 mg dose and 64.5 mg sodium per 1500 mg dose. This is equivalent to 2.58% and 3.23 % of the recommended maximum daily dietary intake of sodium for an adult. However, before Cejemly is given to you, it is mixed with a solution that contains sodium. Talk to your doctor if you are on a low salt diet.

Cejemly contains polysorbate 80
This medicine contains 4.08 mg of polysorbate 80 in each 1200 mg dose and 5.10 mg polysorbate 80 in each 1500 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How you are given Cejemly

How much is given
The recommended dose of Cejemly is 1200 mg for individuals weighing 115 kg or less and 1500 mg for individuals weighing more than 115 kg.

How the medicine is given
Cejemly will be given to you in a hospital or clinic under the supervision of an experienced doctor. You will be given Cejemly through an infusion (drip) into your vein over 60 minutes every 3 weeks.
When Cejemly is given in combination with chemotherapy for your lung cancer; you will first be given Cejemly followed by chemotherapy.

If you miss an appointment
It is very important that you go to all your appointments. If you miss an appointment to receive your medicine, make another one as soon as possible.

4. Possible side effects

Like all medicines, Cejemly can cause side effects, although not everybody gets them. When you are given Cejemly, you can have some serious side effects (see section 2). Your doctor will discuss these with you and will explain the risks and benefits of your treatment.

Seek urgent medical attention if you experience inflammation in any part of your body or if you have any of the following side effects, or if they get worse:

- **Infusion-related reactions** such as chills, shaking or fever, skin problems like itching or rash, flushing or swollen face, trouble breathing or wheezing, nausea, vomiting or abdominal pain (infusion reactions can be severe or life-threatening – these reactions are called anaphylaxis).
- **Problems with hormone-producing glands** such as mood swings, fatigue, weakness, weight fluctuations, changes in blood glucose and cholesterol levels, vision loss, headache that will not go away or unusual headaches, fast heartbeat, increased sweating, feeling more cold or hot than usual, very tired, dizzy or fainting, feeling more hungry or thirsty than usual, hair loss, constipation, your voice gets deeper, very low blood pressure, passing water more often than usual, nausea or vomiting, stomach (abdomen) pain, changes in mood or behaviour (such as decreased sex drive, being irritable or forgetful), inflammation of the adrenal, pituitary or thyroid glands.
- **Signs of diabetes** such as feeling more hungry or thirsty than usual, needing to urinate more often, weight loss, feeling tired or feeling sick, stomach pain, fast and deep breathing, confusion, unusual sleepiness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat.
- **Gut problems** such as frequent diarrhoea often with blood or mucus, more bowel movements than usual, stools that are black or tarry, and severe stomach (abdomen) pain or tenderness (inflammation of the colon).
- **Kidney problems** - passing blood, swollen ankles.

- **Lung problems** such as new or worsening cough, being short of breath or chest pain, inflammation of the lungs (pneumonitis)
- **Liver problems** such as yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on right side of your stomach (abdomen), feeling sleepy, dark urine (the colour of tea), bleeding or bruising more easily than normal and feeling less hungry than usual (inflammation of the liver).
- **Pancreas problems** such as abdominal pain, nausea and vomiting (pancreatitis).
- **Skin problems** such as rash or itching, blisters or ulcers in mouth, nose, eyes and genitals
  - unexplained wide-spread skin pain, red or purple rash that spreads, shedding of the skin within days after blisters form - a severe skin condition called '**Stevens-Johnson syndrome**'.
  - peeling and blistering skin over much of the body - a life-threatening skin condition called '**Toxic epidermal necrolysis**'.

  Heart problems such as changes in heartbeat, heart beating fast, seeming to skip a beat or pounding sensation, chest pain, shortness of breath.
- **Muscle and joint problems** such as joint pain or swelling, muscle pain, weakness, or stiffness.
- **Inflammation of the brain**, which may include fever, headache, movement disorder, neck stiffness.
- **Inflammation of the nerves**, which may include pain, weakness and paralysis in the extremities (Guillain-Barré syndrome)
- **Inflammation of the eyes**, which may include changes in eyesight

Other side effects:

Very common (may affect more than 1 in 10 people):
- decreased number of red blood cells that carry oxygen around your body
- increased levels of liver enzymes, bilirubin in the blood
- increased levels of sugar, triglycerides, cholesterol in the blood
- decreased calcium, potassium, and sodium in the blood
- increased levels of protein in the urine
- numbness, tingling or decreased touch sensation in a part of the body
- fever

Common (may affect up to 1 in 10 people):
- increased levels of uric acid in the blood
- decreased magnesium and/or chloride in the blood
- abnormal liver function
- increased levels of pancreatic enzymes (amylase, lipase)
- inflammation of the nerves causing tingling, numbness, weakness or burning pain of the arms or legs (neuropathy)
- oral mucositis, dry mouth
- increased levels of muscle enzyme (cardiac muscle or skeletal muscle) in the blood
- dry eye, pink eye (conjunctivitis)
- high blood pressure
- increased level of creatinine in the blood
- skin discoloration

Uncommon (may affect up to 1 in 100 people):
- abnormal lipids in the blood
- decreased function of the adrenal gland
- decreased levels of the hormone cortisol in the blood
- inflammation of the blood vessels
- an abnormal reduction in the number of erythrocytes and/or white blood cells

The following side effects have been reported with other similar medicines:

- lack or reduction of digestive enzymes made by the pancreas (pancreatic exocrine insufficiency)
- coeliac disease (characterised by symptoms such as stomach pain, diarrhoea, and bloating after consuming gluten-containing foods)

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Cejemly

Cejemly is stored by the healthcare professionals at the hospital or clinic.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.

Unopened vials: Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

After dilution, an immediate use is recommended. However, from time of preparation by diluting in an intravenous bag, Cejemly can be stored before use for no more than 4 hours at room temperatures up to 25°C, and no more than 24 hours in a refrigerator (2°C to 8°C).

Any unused portion of the infusion solution should be disposed in accordance with local requirements.

6. Contents of the pack and other information

What Cejemly contains
The active substance is sugemalimab. One mL of concentrate for solution for infusion contains 30 mg of sugemalimab. Each 20 mL vial of concentrate for solution for infusion contains 600 mg of sugemalimab.

The other ingredients are histidine, histidine monohydrochloride, mannitol (E421), sodium chloride (see section 2 “Cejemly contains sodium“), polysorbate 80 (E433) (see section 2 “Cejemly contains polysorbate 80”), and water for injections.

What Cejemly looks like and contents of the pack
Cejemly concentrate for solution for infusion is supplied as a clear to opalescent, colourless to slight yellow solution, essentially free from visible particles.

Each carton contains 2 glass vials.

Marketing Authorisation Holder
CStone Pharmaceuticals Ireland Limited
117-126 Sheriff Street Upper
Dublin 1, D01 YC43
Ireland

Manufacturer
Manufacturing Packaging Farmaca (MPF) B.V.
Neptunus 12
8448CN Heerenveen
Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:
AT / BE / CY / DE / DK / EL / ES / FI / FR / IE / IS / IT / LU / MT / NL / NO / PT / SE

CStone Pharmaceuticals Ireland Limited
Ireland
Tel: +353 1 437 0580

Lietuva
Ewopharma UAB
Tel.: +370 5248 7350

Česká republika
Ewopharma, spol. s r. o.
Tel: + 420 2 673 11 613

Eesti
Ewopharma OÜ
Tel: + 372 600 4440

Hrvatska
Ewopharma d.o.o.
Tel: + 385 1 6646 563

Slovenija
Ewopharma d.o.o.
Tel: + 386 590 848 40

Latvija
Ewopharma SIA
Tel: + 371 6770 4000

България
Евофарма ЕООД
Тел.: + 359 2 962 12 00

Magyarország
Ewopharma Hungary Ltd.
Tel.: + 36 1 200 46 50

Polska
Ewopharma AG Sp. z o.o.
Tel.: + 48 22 620 11 71

România
Ewopharma România SRL
Tel: + 40 21 260 13 44

Slovenská republika
Ewopharma spol. s r.o.
Tel: + 421 2 54 79 35 08

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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Instructions for use

Preparation and administration of Cejemly concentrate for solution for infusion

a. Do not shake the vial.

b. **1200 mg dose**
Withdraw 20 mL from each of the 2 vials (total 40 mL) of Cejemly using sterile syringe and transfer into a 250 ml intravenous bag containing sodium chloride 9 mg/mL (0.9%) solution for injection for a total 1200 mg dose. Mix diluted solution by gentle inversion. Do not freeze or shake the solution.
1500 mg dose
Withdraw 20 mL from each of 2 vials and 10 ml from 1 vial (total 50 mL) of Cejemly using sterile syringe and transfer into a 250 ml intravenous bag containing sodium chloride 9 mg/mL (0.9%) solution for injection. Mix diluted solution by gentle inversion. Do not freeze or shake the solution.

c. Do not co-administer other medicinal products through the same infusion line. The infusion solution should be administered through an intravenous line containing a sterile, low-protein binding in-line or add-on polyether sulfone (PES) filter with a 0.22-micron pore size.

d. Allow diluted solution to come to room temperature prior to administration.

e. Discard any unused portion left in the vial.

Storage of diluted solution
Cejemly does not contain a preservative.

Once prepared, 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 4 hours from the time of 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 preparation to the end of infusion. Allow the diluted solution to come to room temperature prior to administration.

Do not freeze.

Disposal
Do not store any unused portion of the infusion solution for re-use. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.