

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.

4.2 Posology and method of administration

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

Posology

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

Recommended dose

For squamous cell carcinoma

Sugemalimab 1200 mg (for individuals weighing 115 kg or less) or 1500 mg (for individuals weighing more than 115 kg) is infused intravenously over 60 minutes followed by intravenous infusion of

carboplatin and paclitaxel on day 1 for up to 4 cycles every 3 weeks. Thereafter, sugemalimab 1200 mg (for individuals weighing 115 kg or less) or 1500 mg (for individuals weighing more than 115 kg) is administered every 3 weeks for the duration of therapy.

For non-squamous cell carcinoma

Sugemalimab 1200 mg (for individuals weighing 115 kg or less) or 1500 mg (for individuals weighing more than 115 kg) is infused intravenously over 60 minutes followed by intravenous infusion of carboplatin and pemetrexed on day 1 for up to 4 cycles every 3 weeks. Thereafter, sugemalimab 1200 mg (for individuals weighing 115 kg or less) or 1500 mg (for individuals weighing more than 115 kg) and pemetrexed are administered every 3 weeks for the duration of therapy.

Sugemalimab is administered in combination with chemotherapy. Refer to the full prescribing information for the combination products (see also section 5.1).

Duration of treatment

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 1.

Table 1. 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	Withhold until the adverse reaction recovers to Grade 0 to 1.

Adverse reaction	Severity*	Treatment modification
	Type-1 diabetes mellitus associated Grade 3 hyperglycaemia	
	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.
	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 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.

* 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 1.

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.

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 hypophysitis) 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, and immune-related rhabdomyolysis/myopathy 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 in combination with chemotherapy has been evaluated in 435 patients receiving 1200 mg every 3 weeks in clinical studies across tumour types.

The incidence of adverse reactions in this patient population was 95.6%. The most common adverse reactions ($\geq 10\%$) were anaemia (77.5%), aspartate aminotransferase increased (34.0%), alanine aminotransferase increased (32.0%), rash (26.2%), hyperlipidaemia (21.6%), hyperglycaemia (18.4%), hyponatraemia (16.8%), hypokalaemia (15.6%), proteinuria (14.0%), abdominal pain (13.8%), fatigue (13.3%), arthralgia (12.2%), hypoaesthesia (11.5%), hypothyroidism (10.3%), 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%), amylase increased (2.1%), hepatic function abnormal (1.8%), hyperglycaemia (1.6%), fatigue (1.4%), rash (1.4%), blood alkaline phosphatase increased (1.1%), and pneumonitis (1.1%).

Tabulated list of adverse reactions

Adverse drug reactions observed in clinical studies of sugemalimab in combination with chemotherapy or sugemalimab monotherapy are listed in Table 2. These reactions are presented by system organ class and by frequency. Frequencies are defined as: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1\ 000$ to $< 1/100$); rare ($\geq 1/10\ 000$ 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 2. Adverse reactions

Blood and lymphatic system disorders	
Very common	anaemia
Uncommon	haemolytic anaemia [#] , immune-related pancytopenia/bicytopenia [*]
Immune system disorders	
Uncommon	anaphylactic reaction, anti-neutrophil cytoplasmic antibody positive vasculitis [#]
Endocrine disorders	
Very common	hypothyroidism
Common	hyperthyroidism
Uncommon	immune-related hypophysitis [*] , adrenal insufficiency, immune-mediated thyroiditis
Metabolism and nutrition disorders	
Very common	hyperlipidaemia ^a , hyperglycaemia ^b , hyponatraemia, hypokalaemia, hypocalcaemia ^c
Common	hyperuricaemia ^d , hypochloraemia ^e , hypomagnesaemia, diabetes mellitus
Uncommon	dyslipidaemia
Nervous system disorders	
Very common	hypoesthesia ^f
Common	neuropathy peripheral
Uncommon	immune-mediated encephalitis, immune-related Guillain-Barre syndrome/demyelination [*]
Eye disorders	
Common	conjunctivitis, dry eye
Cardiac disorders	
Common	tachycardia ^g
Uncommon	immune-mediated myocarditis
Vascular disorders	
Common	Hypertension
Respiratory, thoracic, and mediastinal disorders	

Common	pneumonitis ^h
Gastrointestinal disorders	
Very common	abdominal pain ⁱ
Common	stomatitis ^j , dry mouth
Uncommon	pancreatitis, proctitis, colitis [#]
Hepatobiliary disorders	
Common	hepatic function abnormal, hepatitis ^k
Skin and subcutaneous tissue disorders	
Very common	rash ^l
Common	skin hypopigmentation ^m
Musculoskeletal and connective tissue disorders	
Very common	arthralgia
Common	myalgia, bone pain
Uncommon	myositis [#] , immune-mediated arthritis
Renal and urinary disorders	
Very common	proteinuria ⁿ
Common	nephritis ^o
General disorders and administration site conditions	
Very common	fatigue
Investigations	
Very common	aspartate aminotransferase increased, alanine aminotransferase increased
Common	blood creatinine increased, blood alkaline phosphatase increased, amylase increased, blood bilirubin increased ^p , blood thyroid stimulating hormone increased, blood thyroid stimulating hormone decreased, thyroxine increased ^q , transaminases increased, blood creatine phosphokinase MB increased, thyroxine free decreased, tri-iodothyronine free increased, lipase increased
Uncommon	troponin T increased, cortisol decreased
Injury, poisoning and procedural complications	
Common	infusion related reaction
<p>#Frequency estimate based on incidence in sugemalimab monotherapy study.</p> <p>*Grouped terms which refer to a class effect of immune-related adverse reaction. In clinical studies of sugemalimab in combination with chemotherapy, only myelosuppression, blood corticotrophin decreased, and neuritis were observed respectively under immune-related pancytopenia/bicytopenia, hypophysitis, and Guillain-Barre syndrome/demyelination.</p> <p>The following terms represent a group of related events that describe a medical condition rather than a single event:</p> <ol style="list-style-type: none"> Hyperlipidaemia (hyperlipidaemia, hypercholesterolaemia, hypertriglyceridaemia, blood triglycerides increased) Hyperglycaemia (hyperglycaemia, blood glucose increased) Hypocalcaemia (hypocalcaemia, blood calcium decreased) Hyperuricaemia (hyperuricaemia, blood uric acid increased) Hypochloraemia (hypochloraemia, blood chloride decreased) Hypoaesthesia (hypoaesthesia, anaesthesia) Tachycardia (tachycardia, sinus tachycardia, supraventricular tachycardia, atrial tachycardia, atrial fibrillation, ventricular fibrillation) Pneumonitis (pneumonitis, immune-mediated lung disease, interstitial lung disease) Abdominal pain (abdominal pain, abdominal discomfort, abdominal distension, abdominal pain upper) Stomatitis (stomatitis, mouth ulceration) 	

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|----|---|
| k. | Hepatitis (hepatitis, immune-mediated hepatic disorder, immune-mediated hepatitis, drug-induced liver injury, hepatic failure) |
| l. | Rash (rash, rash maculo-papular, eczema, erythema, dermatitis, dermatitis acneiform, rash erythematous, rash pruritic, urticaria, pruritus, immune-mediated dermatitis) |
| m. | Skin hypopigmentation (skin hypopigmentation, skin depigmentation, leukoderma) |
| n. | Proteinuria (proteinuria, protein urine present) |
| o. | Nephritis (nephritis, renal impairment, renal failure, acute kidney injury) |
| p. | Blood bilirubin increased (blood bilirubin unconjugated increased, bilirubin conjugated increased), |
| q. | Thyroxine increased (thyroxine increased, thyroxine free increased) |

Description of selected adverse reactions

Data for the following immune-related adverse reactions are based on information from 435 patients treated with sugemalimab in combination with chemotherapy 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 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 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).

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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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.

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.

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.

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.

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

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 $\geq 1\%$ (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 $\geq 1\%$, 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/m² 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/m² intravenously administered every 3 weeks for up to 4 cycles followed by sugemalimab 1200 mg and pemetrexed 500 mg/m² 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 3, Figure 1, and Figure 2.

Table 3. 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

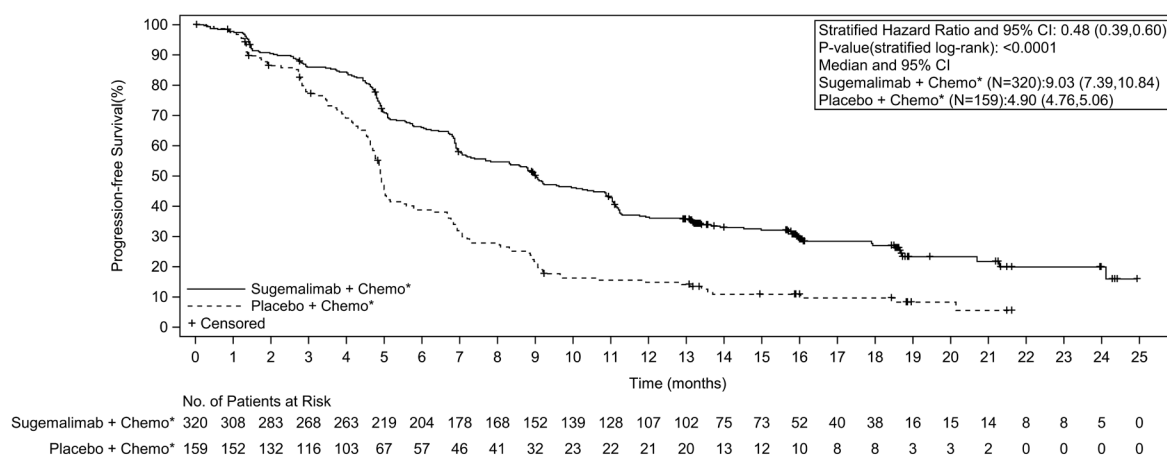


Figure 2. Kaplan-Meier curve of overall survival – ITT population – study GEMSTONE-302

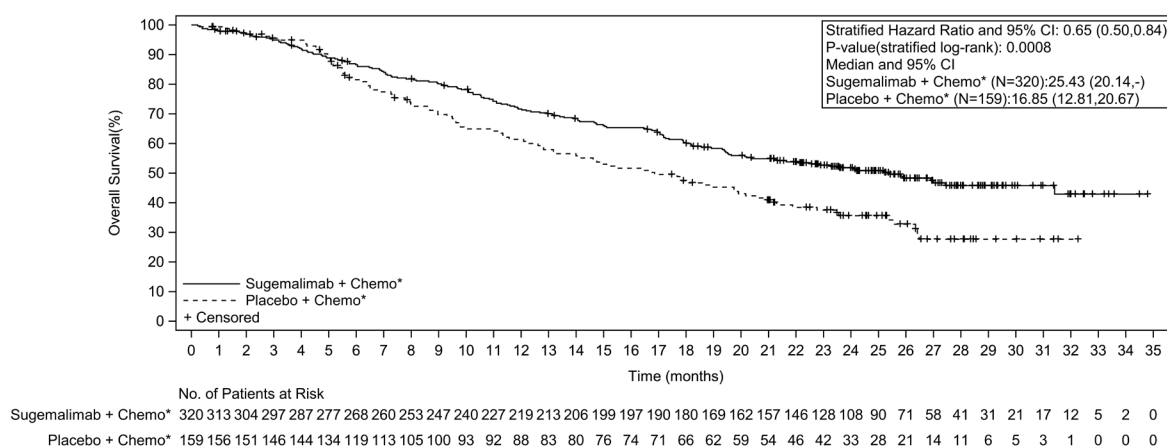
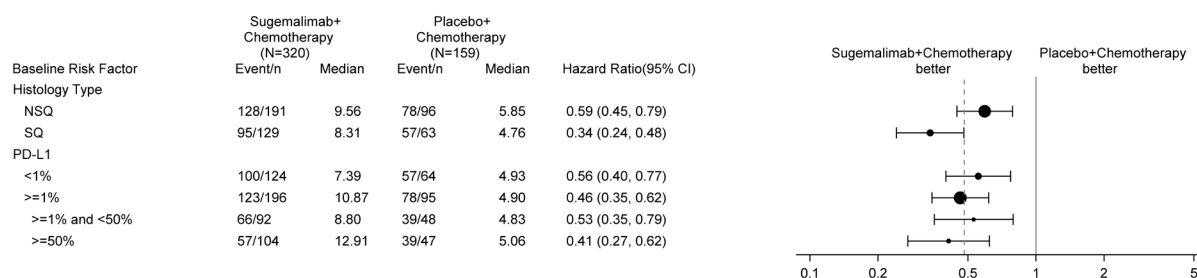


Figure 3. Forest-plot of PFS – study GEMSTONE-302



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.

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 NSCLC study, the prevalence of anti-drug antibodies (ADA) was 17% (53 patients), with 9% (28 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., $R_{acc, C_{max}}$ 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, with a geometric mean (CV%) V_{ss} of 5.56 L (21%) in patients with Stage IV NSCLC from Study GEMSTONE-302.

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%) on NSCLC patients from Study GEMSTONE-302. 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 NSCLC patients from Study GEMSTONE-302.

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 patients with body weight more than 115 kg is anticipated to achieve comparable exposures to the patients in the pivotal study GEMSTONE-302 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
30 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

SFL Pharmaceuticals Deutschland GmbH

Marie-Curie-Strasse 8
79539 Loerrach
Germany

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

<month/year>

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

SFL Pharmaceuticals Deutschland GmbH
Marie-Curie-Strasse 8
79539 Loerrach, Germany

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

SFL Pharmaceuticals Deutschland GmbH

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
2. What you need to know before you use Cejemly
3. How you are given Cejemly
4. Possible side effects
5. How to store Cejemly
6. Contents of the pack and other information

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’ that has spread. Cejemly is used in combination with platinum-based chemotherapy. 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 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.

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 known as AST, ALT in the blood
- increased levels of sugar, triglycerides, cholesterol in the blood
- decreased calcium, potassium, and sodium in the blood
- decreased levels of thyroid hormone in the blood
- increased levels of protein in the urine
- numbness, tingling or decreased touch sensation in a part of the body

Common (may affect up to 1 in 10 people):

- increased levels of uric acid in the blood
- increased level of alkaline phosphatase in the blood
- decreased magnesium and/or chloride in the blood
- increased levels of thyroid hormone in the blood
- abnormal liver function or liver tests
- 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 heart muscle enzyme, in the blood
- dry eye, pink eye (conjunctivitis)
- decreased levels of a hormone called corticotrophin in the blood
- 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

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

SFL Pharmaceuticals Deutschland GmbH
Marie-Curie-Strasse 8
79539 Loerrach
Germany

Manufacturer

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

This leaflet was last revised in <month/year>

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.