Summary Report of Benefit-Risk Assessment

ZERPIDIO (SERPLULIMAB) CONCENTRATE FOR SOLUTION FOR INFUSION 100MG/10ML

NEW DRUG APPLICATION

Active Ingredient(s)	Serplulimab
Product Registrant	Innogene Kalbiotech Pte. Ltd.
Product Registration Number	SIN17246P
Application Route	Abridged evaluation
Date of Approval	29 May 2025

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A INTRODUCTION

Zerpidio in combination with carboplatin and etoposide is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

The active substance, serplulimab, is a recombinant humanised anti-programmed cell death-1 (PD-1) IgG4-type monoclonal antibody and belongs to the pharmacological class of anti-PD-1 inhibitors. It binds to the PD-1 receptor and blocks its interaction with ligands PD-L1 and PD-L2. Serplulimab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands.

Zerpidio is available as concentrate for solution for infusion. One vial of 10 ml of concentrate contains 100 mg of serplulimab. Other ingredients in the vial are citric acid monohydrate, sodium citrate, mannitol, sodium chloride, polysorbate 80, and water for injections.

B ASSESSMENT OF PRODUCT QUALITY

The drug substance, serplulimab, and drug product, Zerpidio Concentrate for Solution for Infusion 100mg/10ml are manufactured at Shanghai Henlius Biopharmaceutical Co., Ltd., Shanghai, PRC.

Drug substance:

Adequate controls have been presented for the intermediates and reagents / cell banks. The in-process control tests and acceptance criteria applied during the manufacturing of the drug substance are considered appropriate. The drug substance manufacturer is compliant with Good Manufacturing Practice (GMP). Process validation was conducted on three consecutive production-scale batches.

The characterisation of the drug substance and its impurities has been appropriately performed. Potential and actual impurities are adequately controlled in the specifications.

The drug substance specifications were established in accordance with ICH Q6A/Q6B guidelines, and the impurity limits have been appropriately qualified. The analytical methods used are adequately described and non-compendial methods have been validated in accordance with ICH Q2 guideline with information on the reference standards used for identity, assay and impurities testing presented.

The packaging is 50L Mobius® storage bag from EMD Millipore. The stability data presented was adequate to support the storage of the drug substance at 5±3°C for 12 months, while protected from light.

Drug product:

The manufacturing process involves pooling and homogenisation of the formulated drug substance, followed by prefiltration, sterile filtration and aseptic filling. This is considered a standard manufacturing process.

The manufacturing site is compliant with GMP. Proper development and validation studies were conducted. It has been demonstrated that the manufacturing process is reproducible and consistent. Adequate in-process controls are in place.

The specifications have been established in accordance with ICH Q6A/ICH Q6B guidelines and impurity limits are considered adequately qualified. The analytical methods used were adequately described and non-compendial methods have been validated in accordance with ICH Q2 guideline with information on the reference standards used for identity, assay and impurities testing presented.

The container closure system is clear Type I glass vial with a 20 mm chlorobutyl rubber stopper. The stability data submitted was adequate to support the approved shelf-life of 36 months when stored at 2-8ºC.

C ASSESSMENT OF CLINICAL EFFICACY

The clinical efficacy of serplulimab in combination with carboplatin and etoposide in the treatment of ES-SCLC was based primarily on one pivotal Phase III study HLX10-005-SCLC301, referred to as the ASTRUM-005 study.

This was a Phase III, randomised, double-blind, multicentre study of serplulimab combined with chemotherapy compared with chemotherapy alone in patients with patients with previously untreated ES-SCLC. Patients in the study were randomised in a 2:1 ratio to receive serplulimab 4.5 mg/kg or placebo via intravenous (IV) infusion over a period of 30 to 90 minutes on Day 1 of each 21-day cycle. Randomisation was stratified by PD-L1 expression level (negative: tumour proportion scores [TPS] <1%, positive: ≥1%, or not evaluable/available), brain metastasis (yes versus no), and age (≥65 versus <65 years). Patients in both arms also received etoposide 100 mg/m^2 via IV infusion on Days 1, 2 and 3 of each cycle as well as carboplatin area under the curve (AUC) = 5, up to a dose of 750 mg via IV infusion on Day 1. Patients received treatment until disease progression, death, intolerable toxicity, withdrawal of informed consent or other reasons specified in the protocol. If a subject had the first disease progression, was clinically stable and intended to receive subsequent second-line chemotherapy, it was at the discretion of the investigator to continue treating with blinded serplulimab or placebo per protocol in addition to the second-line chemotherapy. Although the current preferred standard of care is carboplatin/cisplatin + etoposide + PD-L1 inhibitor (atezolizumab or durvalumab), as there were no approved immunotherapies for the treatment of ES-SCLC at the time of study conduct, placebo with chemotherapy was selected as the comparator, which is acceptable.

The primary efficacy endpoint was overall survival (OS), defined as the time from randomisation to death from any cause. Key secondary efficacy endpoints were progression-free survival (PFS) assessed by the independent radiology review committee (IRRC) based on Response Evaluation Criteria in Solid Tumours (RECIST) 1.1, PFS assessed by the investigator based on RECIST 1.1 and the modified RECIST 1.1 for immune-based therapeutics (iRECIST), objective response rate (ORR) and duration of response (DOR). Subjects underwent computed tomography (CT) or magnetic resonance imaging (MRI) every 6 weeks during the first 48 weeks, and every 9 weeks thereafter.

A total of 585 patients were randomised in the study and were included in the intent-to-treat (ITT) population: 389 patients in the serplulimab arm and 196 patients in the placebo arm. The median age was 62 years (range 28 to 83 years), and the majority of subjects were male (82.2%) and Asian (68.5%). The median duration since the first SCLC diagnosis was 0.23 month, and 97.3% of subjects were diagnosed within 6 months before study entry. At study

entry, almost all (99.8%) subjects had extensive stage SCLC and 80.9% were classified as Stage IV. Nearly all (96.6%) subjects had metastasis, including 13.3% of subjects with CNS metastasis. PD-L1 expression was positive in 16.9% of subjects.

An interim analysis was conducted when 66% of OS events were observed (actual 246 OS events). The efficacy results at interim analysis met the pre-specified stopping boundary. Therefore, a database lock was performed (data cut-off date 22 October 2021) and the study was unblinded.

With a median follow-up duration of 12.3 months, the interim analysis of OS demonstrated a statistically significant improvement for subjects in the serplulimab arm compared to placebo (stratified HR (95% CI): 0.63 (0.489, 0.818); p<0.001). The median OS was 15.4 months in the serplulimab arm compared to 10.9 months in the placebo arm, which was a 4.5-month difference. In the non-Asian and Asian subsets, the stratified HR (95% CI) of OS were 0.70 (0.413, 1.176) and 0.62 (0.458, 0.845), respectively. At interim analysis, the median duration of PFS according to RECIST 1.1 as evaluated by IRRC was 5.7 months in the serplulimab group and 4.3 months in the placebo group (stratified HR (95% CI): 0.48 (0.383, 0.590). In the non-Asian and Asian subsets, the stratified HR (95% CI) were 0.58 (0.391, 0.864) and 0.45 (0.345, 0.585), respectively. In subgroup analyses of OS and PFS by age, sex, race, ethnicity, baseline ECOG performance status score, brain metastasis, and baseline PD-L1 expression levels, the HRs consistently favoured serplulimab over placebo across all subgroups. The subgroup analyses of OS and PFS did not show differential results by PD-L1 expression levels.

The confirmed ORR was 67.4% in the serplulimab group and 58.7% in the placebo group, resulting in an odds ratio (95% CI) of 1.46 (1.022, 2.093). The median duration of confirmed response in patients who had an objective response was 5.78 months in the serplulimab group and 4.14 months in the placebo group. The stratified HR (95% CI) was 0.44 (0.331, 0.582) (p<0.001). A trend of higher HR in the primary and most secondary endpoints was observed in the non-Asian subset compared to Asian subset.

Results of Interim Analysis (ITT)

	Serplulimab (N=389)	**Placebo (N=196)**
OS, overall		
OS events, n (%)	146 (37.5)	100 (51.0)
Median OS (months) (95% CI)	15.38 (13.273, NA)	10.91 (9.955, 14.324)
Stratified Hazard ratio (95% CI) †	0.63 (0.489, 0.818)	
p-value	<0.001	
PFS according to RECIST 1.1 by IRRC		
PFS events, n (%)	223 (57.3)	151 (77.0)
Median PFS (months) (95% CI)	5.72 (5.520, 6.899)	4.34 (4.205, 4.501)
Stratified Hazard ratio (95% CI) †	0.48 (0.383, 0.590)	
p-value	<0.001	
PFS according to RECIST 1.1 by Investigator		
PFS events, n (%)	279 (71.7)	168 (85.7)
Median PFS (months) (95% CI)	5.49 (4.994, 5.684)	4.34 (4.205, 4.435)
Stratified Hazard ratio (95% CI) †	0.58 (0.476, 0.707)	
p-value	<0.001	
PFS according to iRECIST by Investigator		
PFS events, n (%)	260 (66.8)	160 (81.6)
Median PFS (months) (95% CI)	5.68 (5.454, 6.867)	4.37 (4.238, 4.600)
Stratified Hazard ratio (95% CI) †	0.56 (0.454, 0.681)	

p-value	<0.001	
Confirmed# ORR according to RECIST 1.1 by IRRC		
ORR (Complete and partial responses), n (%)	262 (67.4)	115 (58.7)
Odds Ratio (95% CI) *	1.46 (1.022, 2.093)	
Confirmed# DOR according to RECIST 1.1 by IRRC		
Median DOR (months) (95% CI)	5.78 (5.158, 7.524)	4.14 (3.023, 4.205)
Stratified Hazard ratio (95% CI) †	0.44 (0.331, 0.582)	
p-value	<0.001	

Data cut-off date: 22 October 2021
† Stratification factors: PD-L1 expression level (TPS <1%, TPS ≥1%, not evaluable/not available), brain metastasis (yes versus no), and age (≥65 years versus <65 years). The hazard ratio and its 95% CI were estimated by Cox proportional hazards model.
* The odds ratio of ORR and its 95% CI were estimated by the Cochran-Mantel-Haenszel statistics.
# Complete or partial response observed at two consecutive tumour assessments at least 4 weeks apart.

An updated analysis was conducted when 100% of OS events were observed (actual 363 OS events), based on a data cut-off date of 13 June 2022. The O'Brien-Fleming type alpha-spending function (using the Lan-DeMets method to approximate) was used to control overall type I error rate for the multiple analyses.

The OS results in the updated analysis remained similar to the interim analysis. With a median follow-up duration of 19.8 months, the median duration of OS was 15.8 months in the serplulimab group and 11.1 months in the placebo group (stratified HR (95% CI): 0.62 (0.496, 0.763). Similarly, PFS results according to RECIST 1.1 by IRRC was consistent in the updated analysis. The median duration of PFS was 5.75 months in the serplulimab group and 4.34 months in the placebo group (stratified HR (95% CI): 0.47 (0.381, 0.576).

The weight-based dose of serplulimab 4.5 mg/kg every 3 weeks was evaluated in the pivotal clinical study whereas the alternative flat dose of 300 mg every 3 weeks was based on pharmacokinetic (PK) simulation using the population PK model, which showed comparability in terms of AUC_{ss}, $C_{max,ss}$ and $C_{min,ss}$ between the weight-based dose of 4.5 mg/kg and the flat dose of 300mg every 3 weeks.

Overall, the efficacy of serplulimab in combination with carboplatin and etoposide in previously untreated subjects with ES-SCLC was adequately demonstrated in terms of a statistically significant and clinically meaningful improvement in OS compared to carboplatin and etoposide chemotherapy alone.

A controlled, randomised, open-label clinical study (Study NCT05468489) comparing serplulimab with atezolizumab when combined with chemotherapy (carboplatin-etoposide) in previously untreated US patients with ES-SCLC is ongoing. The final results from this study would be required to be submitted to provide additional evidence of efficacy of serplulimab when compared to a current standard of care regimen comprising the PD-L1 inhibitor, atezolizumab, in combination with chemotherapy.

D ASSESSMENT OF CLINICAL SAFETY

The clinical safety of serplulimab was based primarily on safety data derived from the pivotal Phase III ASTRUM-005 study, comprising a total of 585 patients who received at least one dose of study treatment: 389 subjects in the serplulimab arm and 196 subjects in the placebo arm. The median duration of treatment was 22.00 weeks in the serplulimab group and 16.43 weeks in the placebo group. A total of 13.4% of serplulimab subjects remained on treatment as of the data cut-off date (13 June 2022) compared with 3.6% of placebo subjects.

Overview of safety profile

AE	Serplulimab (N=389)	Placebo (N=196)
Any AE	373 (95.9%)	191 (97.4%)
≥Grade 3 AE	310 (79.7%)	151 (77.0%)
Serplulimab/placebo-related AE	273 (70.2%)	113 (57.7%)
SAE	146 (37.5%)	71 (36.2%)
Serplulimab/placebo-related SAE	71 (18.3%)	28 (14.3%)
Discontinuations due to AE	34 (8.7%)	17 (8.7%)
Deaths due to AE	35 (9.0%)	22 (11.2%)

The overall incidence of adverse events (AEs) in the pivotal clinical study was similar between the serplulimab and placebo arms (95.9% vs 97.4%). The most commonly reported AEs included anaemia (serplulimab vs placebo: 71.7% vs 70.9%), neutrophil count decreased (56.3% vs 51.5%), alopecia (54.2% vs 56.6%), white blood cell count decreased (53.7% vs 51.0%), platelet count decreased (41.1% vs 44.9%), nausea (36.2% vs 43.9%), neutropenia (29.6% vs 31.6%), decreased appetite (28.0% vs 28.6%), hyponatraemia (24.7% vs 13.3%), leukopenia (24.4% vs 20.9%), constipation (24.2% vs 29.6%), and vomiting (20.3% vs 29.6%). The types of AEs reported were generally in line with the known safety profile of PD-1/PD-L1 inhibitors when used in combination with chemotherapy.

The rate of AEs leading to death that were considered related to serplulimab/placebo was higher in the serplulimab group (5 patients [1.3%] vs 1 patient [0.5%]). In the serplulimab group, 2 immune-mediated AEs were determined to be related to serplulimab, encephalitis and lung disease. The other serplulimab-related AEs leading to death were acute coronary syndrome, platelet count decreased and pyrexia. SAEs occurred at similar rates between treatment and placebo group (37.5% vs 36.2%) with treatment-related SAEs being higher in the serplulimab group (18.3% vs 14.3%). The most common treatment-related SAEs were platelet count decreased (3.6% vs 5.1%), white blood cell count decreased (2.6% vs 3.1%), and neutrophil count decreased (2.3% vs 5.6%).

The AEs of special interest (AESIs) reported with serplulimab and known to be associated with PD-L1 inhibitors included infusion reactions (1.8% vs 0.5%), immune-related adverse events (irAEs) and immunogenicity.

Immune-related AEs occurred in 37.8% of subjects in the serplulimab group and 19.4% of subjects in the placebo group. The most common irAEs with serplulimab were hypothyroidism (serplulimab vs placebo: 11.8% vs 1.5%), hyperthyroidism (9.3% vs 3.1%), and rash (3.1% vs 1.0%). Five (1.3%) subjects in the serplulimab group had post-treatment positive anti-drug antibody (ADA) results. The AEs of special interest have been adequately described as warnings and precautions in the package insert.

The incidences of treatment-emergent SAEs (Asian 42%, Non-Asian 28%) and AESIs (immune-related AEs: Asian 44%, Non-Asian 24%; infusion reactions: Asian 2.7%, Non-Asian 0) with serplulimab were higher in Asian subjects than in non-Asian subjects. The higher incidence of treatment-emergent SAEs among Asians may reflect differences in response to chemotherapy between Asians and Caucasians. In addition, the incidences of common immune-related AEs in the Asian subset (hypothyroidism 14.9%; hyperthyroidism 11.1%, rash 4.2%), though higher than that in the non-Asian subset, generally fell within the range expected for PD-1/PD-L1 inhibitors and was considered acceptable and manageable. Nonetheless, the comparisons between the serplulimab and placebo groups were similar in the Asian subset

(SAEs: 42.4% vs 38.1%, irAEs: 44.3% vs 23.0%) as well as the non-Asian subset (SAEs: 27.6% vs 31.6%, irAEs: 24.4% vs 10.5%).

The safety profile of serplulimab was comparable to that of other anti-PD-1/PD-L1 antibodies used for the treatment of ES-SCLC. Overall, the toxicities reported with serplulimab given in combination with carboplatin and etoposide were consistent with the regimen components and the mitigation measures which included a patient medication guide and warnings in the package insert were considered adequate.

E ASSESSMENT OF BENEFIT-RISK PROFILE

ES-SCLC is highly aggressive, with a tendency to spread quickly to distant sites and a five-year survival rate of less than 7%. The current standard of care for first-line treatment of ES-SCLC is atezolizumab or durvalumab in combination with the chemotherapy regimen of a platinum plus etoposide. Considering the aggressive disease progression and limitations of current treatment for ES-SCLC, there remains a place for additional therapies to expand the treatment options for patients.

In the pivotal study ASTRUM-005, treatment with serplulimab in combination with carboplatin and etoposide in patients with previously untreated ES-SCLC was associated with a significant reduction in the risk of death by 37% and an improved survival by a median of 4.5 months compared to chemotherapy alone (HR 0.63; 95% CI: 0.489, 0.818). The efficacy of serplulimab was also supported by the secondary endpoints, including PFS, ORR, and DOR. Notwithstanding the limitations of cross-study comparisons, the efficacy results were generally consistent with that reported with other PD-L1 monoclonal antibodies, atezolizumab and durvalumab.

The safety profile of serplulimab was characterised by hematologic and immune-related AEs, which was consistent with other PD-1/PD-L1 inhibitors used in the treatment of ES-SCLC. The AEs of special interest reported with serplulimab were primarily infusion reactions and irAEs including hypothyroidism, hyperthyroidism and rash. These risks have been adequately addressed in the local package insert via the provision of relevant warnings and precautions, as well as dose adjustment recommendations in the event of toxicities. To ensure adequate risk mitigation, the risk management plan (RMP) has included a patient medication guide for educating patients about irAEs and infusion reactions.

Overall, the benefit-risk profile of serplulimab given in combination with carboplatin and etoposide in patients with previously untreated ES-SCLC was considered favourable.

F CONCLUSION

Based on the review of quality, safety and efficacy data, the benefit-risk balance of Zerpidio in combination with carboplatin and etoposide for the first-line treatment of adult patients with ES-SCLC was deemed favourable and approval of the product registration was granted on 29 May 2025. The approval of this application is subject to the submission of the final study report of the ongoing controlled study NCT05468489 to support the clinical benefit and demonstrate a favourable overall risk-benefit profile.

APPROVED PACKAGE INSERT AT REGISTRATION

Zerpidio

Concentrate Solution for Infusion

Composition
Each mL of concentrate for solution for infusion contains 10 mg of serplulimab.
One vial of 10 mL of concentrate contains 100 mg of serplulimab.

Serplulimab is a humanised monoclonal anti-programmed cell death -1 (PD-1) antibody produced in Chinese hamster ovary cells by recombinant DNA technology.
Excipient(s) with known effect
It contains 22.5 mg of sodium (main component of cooking/table salt) in each unit volume. This is equivalent to 1.1% of the recommended maximum daily dietary intake of sodium for an adult.

List of excipients
Citric acid monohydrate
Sodium citrate dihydrate
Sodium chloride
Mannitol
Polysorbate 80
Water for injection

Pharmaceutical form
Concentrate for solution for infusion (sterile concentrate). Colourless to slightly yellow, clear to slightly opalescent liquid

Therapeutic Indications
Zerpidio in combination with carboplatin and etoposide is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Pharmacological Properties
Pharmacodynamic properties
Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies and antibody drug conjugates, PD-1/PD-L1 (Programmed cell death-1/ death ligand 1) inhibitors.
ATC code: L01FF12

Mechanism of action
Serplulimab is a humanised monoclonal antibody which binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with ligands PD-L1 and PD-L2. The PD-1 receptor is a negative regulator of T-cell activity that has been shown to be involved in the control of T-cell immune responses. Engagement of PD-1 with the ligands PD-L1 and PD-L2, which are expressed in antigen presenting cells and may be expressed by tumours or other cells in the tumour microenvironment, results in inhibition of T-cell proliferation and cytokine secretion. Serplulimab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands. In syngeneic mouse models, blocking PD-1 activity resulted in decreased tumour growth.
The PD-1 receptor occupation of peripheral T cells and interleukin-2 (IL-2) release ability in vitro were studied in the phase 1 study involving 29 Chinese patients with advanced solid tumour that were injected with single and multiple doses (0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg) of serplulimab. The result shows that serplulimab could stably maintain the saturation state of receptor occupation and sustained functional blockage at the dosage from 0.3 mg/kg to 10 mg/kg every 2 weeks interval.

Clinical efficacy and safety
The efficacy of serplulimab (HLX10) in combination with chemotherapy (carboplatin plus etoposide) for the treatment of previously untreated ES-SCLC was evaluated in HLX10-005-SCLC301 study, a phase 3, randomised, double-blind, multiregional clinical trial. The primary efficacy endpoint was overall survival (OS). Secondary efficacy endpoints were progression free survival (PFS), objective response rate (ORR) and duration of response (DOR) as assessed by independent radiology review committee (IRRC) and investigator based on RECIST 1.1.
A total of 585 patients were enrolled. Three hundred eighty-nine (389) patients received serplulimab in combination with chemotherapy treatment, and 196 patients received placebo in combination with chemotherapy treatment. Among the patients enrolled, 68.5% were Asian (401 patients), and 31.5% were non-Asian (184 patients), all of them were Caucasian.
As of 22 October 2021, the median duration of follow-up in the overall ITT population was 12.32months. In the serplulimab group and the placebo group, the median OS was 15.38 months (95%CI: 13.273, not assessable) and 10.91 months (95% CI: 9.955, 14.324), respectively; with a HR of 0.63(95% CI: 0.489, 0.818), p<0.001. The primary endpoint reached prespecified statistical significance (alpha: 0.012) in the interim analysis. The median OS showed an improvement of 4.47 months in the serplulimab group.
In the updated analysis with longer follow up duration (median: 19.75 months) by the cutoff date 13 June 2022, the median OS (95% CI) was 15.80 (14.127, 17.577) months in the serplulimab group and 11.10 (9.955, 12.353) months in the placebo group. The stratified HR (95% CI) was 0.62 (0.496, 0.763) with p value < 0.001. Treatment with serplulimab reduced the risk of death by 38% and prolonged the duration of survival by a median of 4.70 months. The 2-year OS rate (95% CI) in the serplulimab group and the placebo group was 31.7% (25.6%, 37.9%) and 18.7% (12.5%, 25.9%), respectively.
In the serplulimab group and the placebo group, the median PFS (95% CI) by IRRC assessment per RECIST 1.1 was 5.75 (5.552, 6.932) months and 4.34 (4.205, 4.435) months, respectively; with a stratified HR (95% CI) of 0.47 (0.381, 0.576), p < 0.001. Compared with the placebo group, serplulimab group reduced the risk of disease progression or death by 53%.
In the PD-L1 TPS ＜1% subgroup, the median OS (95% CI) was 15.9 (13.90, 17.58) months in the serplulimab group, and 10.5 (8.64, 12.32) months in the placebo group (HR of 0.59, 95% CI: 0.470, 0.752). In the PD-L1 TPS ≥1% group, the median OS (95% CI) was 14.9 (11.63, NA) months in the serplulimab group, and 12.9 (9.72, NA) months in the placebo group (HR of 0.76, 95% CI: 0.424, 1.375).
In the PD-L1 TPS ＜1% subgroup, the median PFS (95% CI) by IRRC assessment per RECIST 1.1 was 5.7 (5.49, 6.93) months in the serplulimab group and 4.3 (4.17, 4.40) months in the placebo group (HR of 0.47, 95% CI: 0.376, 0.591). In the PD-L1 TPS ≥1% group, the median PFS (95% CI) by IRRC assessment per RECIST 1.1 was 6.3 (5.39, 9.66) months in the serplulimab group and 5.5 (4.34, 5.98) months in the placebo group (HR of 0.62, 95% CI: 0.379, 1.022).
In the serplulimab group and the placebo group, the confirmed ORR was 68.9% and 58.7%, respectively; and the median DOR was 6.47 months and 4.17 months, respectively.
A summary of efficacy data in HLX10-005-SCLC301 is shown in Table 1. Kaplan-Meier curve of OS in overall ITT population is presented in Figure 1. Kaplan-Meier curve of PFS by IRRC assessment based on RECIST 1.1 in overall population is presented in Figure 2.

Table 1. Efficacy Data of HLX10-005-SCLC301 (Data cut-off date: 13 June 2022)

Population		Global (n=585)	non-Asian (n=184)	Asian (n=401)
Number of patients (serplulimab group vs placebo group)		389 vs 196	127 vs 57	262 vs 139
Median follow-up (months)		19.75	16.10	21.03
Primary endpoint				
OS	Number of event (Deaths), n (%)	363 (62.1%)	105 (57.1%)	258 (64.3%)
	Median OS (months)	**15.80 vs 11.10**	**15.64 vs 11.20**	**15.90 vs 11.10**
	Hazard Ratio (95% CI)	**0.62 (0.496, 0.763)**	**0.51 (0.334, 0.791)**	**0.65 (0.505, 0.840)**
	p-Value	< 0.001	0.002	< 0.001
	2-year OS rate (%)	31.7% vs 18.7%	26.3% vs 10.2%	33.1% vs 20.2%
Secondary endpoints				
PFS	Median PFS (months)	5.75 vs 4.34	5.65 vs 5.03	6.08 vs 4.27
	Hazard Ratio (95% CI)	0.47 (0.381, 0.576)	0.54 (0.373, 0.791)	0.45 (0.353, 0.585)
IRRC per RECIST 1.1	p-Value	< 0.001	0.001	< 0.001

Population		Global (n=585)	non-Asian (n=184)	Asian (n=401)
Confirmed				
ORR	(%)	68.9% vs 58.7%	63.0% vs 59.6%	71.8% vs 58.3%
DOR	Median DOR (months)	6.47 vs 4.17	5.55 vs 4.17	6.93 vs 3.22

Figure 1. Kaplan-Meier Curve of Overall Survival in Overall Population (ITT)

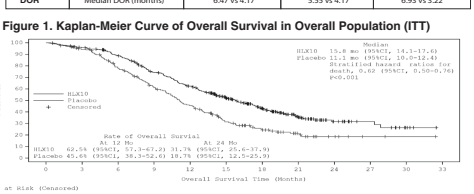
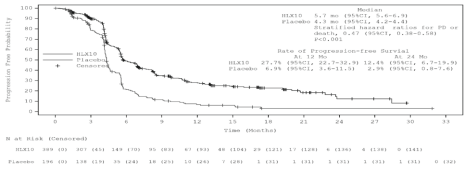


Figure 2. Kaplan-Meier Curve of Progression Free Survival (RECIST 1.1) by IRRC (ITT) in Overall population (ITT)



Elderly patients
In the study HLX10-005-SCLC301 of the 389 patients in the serplulimab group in the efficacy population, 153 (39.3%) were older than 65 years. No major differences in efficacy were observed between elderly patients and younger patients.

Pharmacokinetic properties
The pharmacokinetic data of serplulimab comes from the results of a population pharmacokinetic analysis of 2110 patients included in 11 clinical studies of patients with a variety of cancers including small cell lung cancer, squamous non-small cell lung cancer, non-squamous non-small cell lung cancer, esophageal squamous cell carcinoma, microsatellite instability-high solid tumors, hepatocellular carcinoma, cervical carcinoma , head and neck tumors, and colorectal cancer.

In the study HLX10-005-SCLC301 for ES-SCLC patients, the mean C_{max} of serplulimab was 85.44 μg/mL and 152.63 μg/mL after single-dose and steady state, respectively. The mean C_{trough} was 21.49 μg/mL and 62.47 μg/mL after single-dose and steady state, respectively. Serplulimab exhibited linear pharmacokinetics over the dose range of 0.3 to 10 mg/kg Q2W both after single and multiple doses.

Absorption
Zerpidio is administered via intravenous route and therefore is immediately and completely bioavailable. There have been no studies performed with other routes of administration.
Distribution
A population pharmacokinetic analysis indicates that the central compartment volume of distribution (V_c) of serplulimab in patients ranges from 3.19 to 3.48 L, with an inter-individual variability of 16.3%; the peripheral compartment volume of distribution (V_p) is 2.98 L, with an inter-individual variability of 45.9%.
Metabolism
Serplulimab is expected to be catabolized into amino acids by general protein degradation process. Metabolism studies are generally not performed for biologic products such as serplulimab, because these products are proteins which are degraded into amino acids that are then recycled into other proteins.
Elimination
The baseline clearance (CL_0) of serplulimab in patients ranges from 0.171 to 0.211 L/day, with an inter-individual variation of 24.0%, based on the population PK analysis. The clearance gradually decreased with the administration time, the maximum proportional change in clearance from baseline is 0.912 and the time to reach the half of the maximum change in clearance is 221 days. The median half-life after the first dose and at steady state are 19.0 and 24.4 days, respectively.
Simulation of PK exposure comparison between 4.5 mg/kg Q3W and 300 mg Q3W
The 4.5 mg/kg every 3 week dose was evaluated in clinical studies, with flat dose of 300mg every 3 weeks derived using modelling and simulation based on the population PK model. The comparison of PK parameters ($C_{max,ss}$, $C_{min,ss}$ and AUC_{ss}) between the doses of 4.5 mg/kg every 3 weeks and 300 mg every 3 weeks is present in below table.

Exposures	Geometric mean (CV%)		Change (%)*
	4.5 mg/kg Q3W	300 mg Q3W	
AUC_{ss} (μg*day/mL)	1598.7 (26.7)	1703.99 (27.4)	6.59
$C_{max,ss}$ (μg/mL)	138.19 (19.7)	147.29 (20.9)	
$C_{min,ss}$ (μg/mL)	50.8 (34.4)	54.15 (35.9)	

*Change= (300 mg - 4.5 mg/kg)/(4.5 mg/kg)*100

Preclinical safety data
Genotoxicity
No study has been performed to assess the potential of Zerpidio for genotoxicity.

Reproductive Toxicity
The reproductive toxicity of Zerpidio has not been studied. In 3- and 6-month repeat-dose toxicology studies in cynomolgus monkeys, there were no notable effects in the male and female reproductive organs; however, most animals in these studies were not sexually mature.
One of the main functions of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the foetus. In murine models of pregnancy, blockade of PD-L1 signalling has been shown to disrupt tolerance to the foetus and to result in an increase in foetal loss; therefore, potential risks of administering Zerpidio during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-1/PD- L1 signalling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, foetal exposure to Zerpidio may increase the risk of developing immune-mediated disorders or altering the normal immune response.

Carcinogenicity
No studies have been performed to assess the potential of Zerpidio for carcinogenicity.

Other toxicity
In animal models, inhibition of PD-L1/PD-1 signalling increased the severity of some infections and enhanced inflammatory responses. Mycobacterium tuberculosis-infected PD-1 knockout mice exhibit markedly decreased survival compared with wild-type controls, which correlated with increased bacterial proliferation and inflammatory responses in these animals. PD-L1 and PD-1 knockout mice have also shown decreased survival following infection with lymphocytic choriomeningitis virus.

Contraindications
Hypersensitivity to active substance or to any of the excipients listed in section **List of excipients.**

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

Posology
The recommended dose of Zerpidio is 4.5 mg/kg every 3 weeks or 300 mg every 3 weeks* until disease progression or unacceptable toxicity.
Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months of treatment, followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until disease progression is confirmed.
Dose escalation or reduction of Zerpidio is not recommended. Dose withholding or discontinuation may be required based on individual safety and tolerability.
Guidelines for management of immune-related adverse reactions are described in Table 2 (see section **Special Warnings and Precautions for Use)**.
*The recommended alternative flat dosing of 300 mg every 3 weeks has not been investigated in patients with ES-SCLC and is based on population pharmacokinetic modelling and simulations.

Table 2. Recommended treatment modifications for Zerpidio

Immune -related adverse reactions	Severity	Treatment modification
Immune-related lung disease	Grade 2	Withhold until adverse reactions recover to Grade 0-1
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue
Colitis	Grade 2 or 3	Withhold until adverse reactions recover to Grade 0-1
	Grade 4 or recurrent Grade 3	Permanently discontinue
Hepatitis	Grade 2 with AST or ALT > 3 to 5 times ULN or total bilirubin > 1.5 to 3 times ULN	Withhold until adverse reactions recover to Grade 0-1
	Grade 3 or 4 with AST or ALT > 5 times ULN, or total bilirubin > 3 times ULN	Permanently discontinue
Nephritis and renal dysfunction	Grade 2 elevation of serum creatinine	Withhold until adverse reactions recover to Grade 0-1
	Grade 3 or 4 elevation of serum creatinine	Permanently discontinue
Endocrinopathies	Symptomatic Grade 2 or 3 hypothyroidism, Grade 2 or 3 hyperthyroidism, Grade 2 or 3 hypophysitis, Grade 2 adrenal insufficiency, Grade 3 hyperglycaemia or type 1 diabetes mellitus	Withhold until adverse reactions recover to Grade 0-1
	Grade 4 hypothyroidism Grade 4 hyperthyroidism Grade 3 or 4 adrenal insufficiency Grade 4 hyperglycaemia	Permanently discontinue
Skin adverse reactions	Grade 3	Withhold until adverse reactions recover to Grade 0-1
	Grade 4, Stevens Johnson Syndrome (SJS) or toxic epidermal necrolysis (TEN)	Permanently discontinue
Other immune-related adverse reactions	Grade 3 or 4 elevation of serum amylase or lipase Grade 2 or 3 pancreatitis Grade 2 myocarditis* Grade 2 or 3 other immune-mediated adverse reactions occurred for the first time Grade 3 Decreased platelet count (thrombocytopenia) or white blood cell count	Withhold until adverse reactions recover to Grade 0-1
	Grade 4 pancreatitis or recurrent pancreatitis of any grade Grade 3 or 4 myocarditis Grade 3 or 4 encephalitis Grade 4 other immune-related adverse reactions occurred for the first time Grade 4 or recurrent Grade 3 Decreased platelet count (thrombocytopenia) or white blood cell count	Permanently discontinue
Infusion-related reactions	Grade 2	Reduce infusion rate or interrupt. Treatment may be resumed when the event is resolved
	Grade 3 or 4	Permanently discontinue

Note: Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0).
ALT: alanine aminotransferase; AST: aspartate aminotransferase; ULN: upper limit of normal
*The safety of Zerpidio is not clear when myocarditis is improved to Grade 0-1.

Special Populations
Paediatric population
The safety and efficacy of Zerpidio in children and adolescents below 18 years of age have not been established. No data are available.
Elderly
No dose adjustment is required for elderly patients (≥ 65 years). Zerpidio must be administered with caution in this population.
Renal impairment
No dose adjustment is needed for patients with mild (CRCL=60-89mL/min) or moderate (CRCL=30-59 mL/min) renal impairment. There are insufficient data in patients with severe (CRCL=15-29 mL/min) renal impairment for dosing recommendations.
Hepatic impairment
No dose adjustment is needed for patients with mild (BIL ≤ ULN and AST > ULN or BIL > 1 to 1.5 × ULN and any AST*) hepatic impairment. There are insufficient data in patients with moderate (BIL > 1.5 to 3 × ULN and any AST*) hepatic impairments and no data are available in severe (BIL > 3 × ULN and any AST*) hepatic impairments for dosing recommendations.
*Hepatic impairment is not defined solely based on BIL and AST levels.

Method of administration
Zerpidio is for intravenous use.
The initial infusion rate should be set up to 100 mL per hour. If the first infusion is well tolerated, all subsequent infusions may be shortened to 30 minutes.
Preparation and administration
- Confirm the dose of the product and calculate the required volume of Zerpidio.
- To make a total volume of 100 mL, use a sterile syringe to extract the normal saline (100 mL of 0.9% sodium chloride solution) at the volume which equals to the required Zerpidio volume and discard it.
- Use a syringe to withdraw the required volume of Zerpidio from the vial and inject it into normal saline.
- Set the initial infusion rate to 100 mL per hour (25 drops per minute is recommended, and the infusion rate can be adjusted if infusion related reactions occur). If there is no infusion related adverse reactions in the first infusion, the duration of subsequent administration can be shortened to 30 minutes.
- At the end of infusion, the infusion tube is flushed with normal saline according to the routine operation procedure of the hospital.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. Zerpidio should not be infused concomitantly in the same intravenous line with other medicinal products.

Diluted solution
From a microbiological point of view, the prepared solution for infusion 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 no longer than 24 hours at 2 °C-8 °C. The 24-hour hold may include up to 6 hours at room temperature (≤ 25°C). Aseptic handling should be ensured during the preparation of infusion.

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
Serplulimab is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance, and inducing immune- mediated adverse reactions. Important immune-related adverse reactions listed in this section may not include all possible severe and fatal immune-related reactions.
Immune-related adverse reactions, including severe and fatal cases, have occurred in patients receiving Zerpidio. Most immune-related adverse reactions occurring during treatment with serplulimab were reversible and managed with interruptions of serplulimab, administration of corticosteroids and/or supportive care. Immune-related adverse reactions have also occurred after the last dose of serplulimab. Immune-related adverse reactions affecting more than one body system can occur simultaneously. For suspected immune-related adverse reactions, adequate evaluation to confirm aetiology or exclude other causes should be ensured. Based on the severity of the adverse reaction, Zerpidio should be withheld and corticosteroid administered. For most Grade 2 and some specific Grade 3 or 4 immune-related adverse reactions, serplulimab should be withheld until improvement to Grade 0-1. Zerpidio must be permanently discontinued for any Grade 4 and some specific Grade 3 immune-related adverse reactions. For Grade 3, 4 and some specific Grade 2 immune-related adverse reactions, corticosteroid (1-2 mg/kg/day prednisone or equivalent) and other treatments should be given according to the clinical symptoms until improvement to Grade 0-1. Upon improvement to Grade ≤ 1, corticosteroid taper should be initiated and continued over at least 1 month. Rapid tapering may lead to worsening or recurrence of the adverse reaction. Non-corticosteroid immunosuppressive therapy should be added if there is worsening or no improvement despite corticosteroid use.
Serplulimab must be permanently discontinued for any Grade 3 immune-related adverse reaction that recurs and for Grade 2 or 3 immune-related adverse reactions that did not recover to Grade ≤1 (except endocrinopathies) within 12 weeks after last dose of serplulimab, and for corticosteroids could not be reduced to ≤ 10 mg/day prednisone or equivalent within 12 weeks after last of serplulimab (see section **Posology and Method of Administration).**

Immune-mediated encephalitis
Immune-related encephalitis has been reported in patients treated with Zerpidio including fatal cases (see section **Undesirable Effects**). Patients should be monitored for clinical signs and

symptoms of encephalitis. Suspected immune-mediated encephalitis should be confirmed with specific examinations and other causes excluded. For Grade 3 or 4 encephalitis, Zerpidio must be permanently discontinued and corticosteroids therapy should be initiated (see section **Posology and Method of Administration**).

Immune-related lung disease
Immune-related pneumonitis has been reported in patients receiving serplulimab (see section **Undesirable Effects**). Patients should be monitored for signs and symptoms of immune-related pneumonitis. Suspected immune-related pneumonitis should be confirmed with radiographic imaging and other causes excluded. Serplulimab should be withheld for Grade 2 immune-related pneumonitis, and permanently discontinued for Grade ≥ 3 or recurrent Grade 2 immune-related pneumonitis (see section **Posology and Method of Administration**).

Immune-related colitis
Immune-related colitis has been reported in patients receiving serplulimab (see section **Undesirable Effects**). Patients should be monitored for signs and symptoms of immune-related colitis, such as abdominal pain, diarrhoea, mucus, or blood in stool. Infection and other disease-related aetiologies should be ruled out.
Zerpidio should be withheld for Grade 2 or 3 immune-related colitis, and permanently discontinued for Grade 4 or recurrent Grade 3 immune-mediated colitis (see section **Posology and Method of Administration**). The potential risk of gastrointestinal perforation should be taken into consideration and confirmed by radiographic imaging and/or endoscopy if necessary.

Immune-related hepatitis
Immune-related hepatitis has been reported in patients receiving Zerpidio, including fatal cases (see section **Undesirable Effects**). Patients should be monitored for abnormal liver tests prior to initiation of treatment, changes in liver function and clinical signs and symptoms of immune-related hepatitis periodically (every month). Infection and diseases-related aetiologies should be ruled out. The frequency of liver function test should be increased, if immune- related hepatitis occurs. Zerpidio should be withheld for Grade 2 immune-related hepatitis, and permanently discontinued for Grade 3 or 4 immune-related hepatitis (see section **Posology and Method of Administration**).

Immune-related nephritis and renal dysfunction
Immune-related nephritis and renal dysfunction have been reported in patients receiving Zerpidio (see section **Undesirable Effects**). Patients should be monitored for changes in renal function and clinical signs and symptoms of immune-related nephritis and renal dysfunction periodically (every month). The frequency of renal function test should be increased, if immune-related nephritis occurs. Most patients present with asymptomatic increases in serum creatinine. Disease-related aetiologies should be ruled out. Zerpidio should be withheld for Grade 2 serum creatinine elevation, and permanently discontinued for Grade 3 or 4 serum creatinine elevation (see section **Posology and Method of Administration**).

Immune-related endocrinopathies
Thyroid Diseases
Thyroid disorders, including hyperthyroidism, hypothyroidism, thyroiditis, and goitre have been reported in patients receiving serplulimab (see section **Undesirable Effects**). Patients should be monitored for abnormal thyroid function tests prior to initiation of treatment, changes in thyroid function and clinical signs and symptoms of thyroid disorders. For Grade 2 or 3 symptomatic hypothyroidism, serplulimab should be withheld and thyroid hormone replacement should be initiated as needed. For Grade 2 or 3 symptomatic hyperthyroidism, serplulimab should be withheld and anti-thyroid medicinal product should be initiated as needed. If acute inflammation of the thyroid is suspected, serplulimab should be withheld and initiate hormone therapy. Treatment with serplulimab may be resumed when symptoms of hypothyroidism or hyperthyroidism are controlled, and thyroid function is improved. For life-threatening hyperthyroidism or hypothyroidism, serplulimab must be permanently discontinued. Thyroid function should be monitored continuously to ensure appropriate hormone replacement (see section **Posology and Method of Administration**).

Pituitary disorders
Hypophysitis has been reported in patients receiving serplulimab (see section **Undesirable Effects**). Patients should be monitored for signs and symptoms of hypophysitis, and other causes should be ruled out. For Grade 2 or 3 symptomatic hypophysitis, serplulimab should be withheld and hormone replacement should be initiated as needed. If acute hypophysitis is suspected, corticosteroids should be initiated. For life-threatening Grade 4 hypophysitis serplulimab must be permanently discontinued.

Adrenal insufficiency
Adrenal insufficiency has been reported in patients receiving serplulimab (see section **Undesirable Effects**). Patients should be monitored for signs and symptoms, and other causes should be ruled out. For Grade 2 Adrenal insufficiency serplulimab should be withheld and hormone replacement should be initiated as needed. For life-threatening Grade 3 or 4 adrenal insufficiency, serplulimab must be permanently discontinued. Adrenal gland function and hormone levels should be monitored continuously to ensure appropriate hormone replacement (see section **Posology and Method of Administration**).

Hyperglycaemia
Hyperglycaemia or type 1 diabetes mellitus has been reported in patients receiving serplulimab (see section **Undesirable Effects**). Patients should be monitored for blood glucose level and related clinical signs and symptoms. Insulin replacement therapy should be initiated as needed. For type 1 diabetes mellitus with poor blood glucose control, serplulimab should be withheld, and insulin replacement therapy should be initiated until the symptoms are improved. For life-threatening Grade 4 type 1 diabetes, serplulimab must be permanently discontinued. Blood glucose levels should be monitored continuously to ensure appropriate insulin replacement (see section **Posology and Method of Administration**).

Immune-related adverse skin reactions
Immune-related skin adverse reactions have been reported in patients receiving Zerpidio (see section **Undesirable Effects**). For Grade 1 or 2 rash, the treatment of Zerpidio can be continued, and symptomatic treatment or local corticosteroids treatment can be given. For Grade 3 rash, Zerpidio should be withheld, and symptomatic treatment or local corticosteroids treatment should be given. For Grade 4 rash, Stevens-Johnson syndrome (SJS), or toxic epidermal necrolysis (TEN), Zerpidio should be permanently discontinued (see section **Posology and Method of Administration**).

Immune-related pancreatitis
Immune-related pancreatitis, including increases in serum amylase and lipase levels, has been reported in patients receiving serplulimab, including fatal cases (see section **Undesirable Effects**). Patients should be monitored for changes in serum lipase and amylase (at the beginning of treatment, periodically during treatment and as indicated based on clinical evaluation), and clinical signs and symptoms of pancreatitis. Serplulimab should be withheld for Grade 3 or 4 serum amylase or lipase levels increased, and Grade 2 or 3 pancreatitis. For Grade 4 pancreatitis or recurrent pancreatitis of any grade, serplulimab should be permanently discontinued (see section **Posology and Method of Administration**).

Immune-related myocarditis
Immune-related myocarditis has been reported in patients receiving treated with Zerpidio including fatal cases (see section **Undesirable Effects**). Patients should be monitored for clinical signs and symptoms of myocarditis. Suspected immune-mediated myocarditis should be confirmed with myocardial enzyme spectrum examinations and other causes excluded. For Grade 2 myocarditis, Zerpidio should be withheld, and corticosteroid treatment should be given. The safety of restarting Zerpidio treatment after myocarditis recovered to Grade 0 or 1 is unclear. For Grade 3 or 4 myocarditis, Zerpidio must be permanently discontinued and corticosteroids therapy should be initiated. Myocardial enzymes and cardiac function should be monitored closely (see section **Posology and Method of Administration**).

Other Immune-related adverse reactions
Given the mechanism of action of Zerpidio, other potential immune-related adverse reactions may occur. The following immune-related adverse reactions were reported in less than 1% of patients treated with Zerpidio in clinical trials across doses and tumour types: ventricular extrasystole, herpes zoster, hyperuricemia, mouth ulceration, nausea, and vomiting, etc. (see section **Undesirable Effects**).
For other suspected immune-related adverse reactions, adequate evaluation should be performed to confirm aetiology and exclude other causes. Based on the severity of adverse reactions, Zerpidio should be withheld for Grade 2 or 3 immune-related adverse reactions which occur at first time. For recurrent Grade 3 immune-related adverse reactions (except endocrinopathies) and Grade 4 immune- related adverse reactions, Zerpidio must be permanently discontinued. Corticosteroids can be initiated as clinically indicated (see section **Posology and Method of Administration**).
If uveitis and other immune-mediated adverse reactions occur at the same time, such as Vogt-Koyanagi- Harada syndrome, systemic corticosteroids should be given to prevent permanent blindness.
The following additional clinically significant immune-mediated adverse reactions were reported in patients treated with other PD-1/PD-L1 blocking antibodies: aplastic anaemia and exocrine pancreatic insufficiency.

Infusion-related reactions
Infusion-related reactions have been reported in patients receiving Zerpidio. Patients should be monitored for clinical signs and symptoms of infusion-related reactions. Patients with Grade 1 infusion-related reaction may continue to receive Zerpidio close monitoring. The rate of infusion should be reduced, or treatment should be interrupted in patients with Grade 2 infusion-related reaction. Antipyretic and antihistamines may be considered. Treatment with Zerpidio may be resumed with close monitoring when symptoms of infusion-related reaction are controlled. For Grade ≥ 3 infusion-related reaction, infusion should be stopped immediately and Zerpidio permanently discontinued, and appropriate treatment should be given (see section **Posology and Method of Administration**).

Patients excluded from clinical trials
Patients with the following conditions were excluded from clinical trials: a history of active or prior documented autoimmune disease, patients with active tuberculosis or hepatitis B or C or HIV infection or patients receiving live attenuated vaccine within 28 days prior to study drug administration, patients with any active infection requiring systemic anti-infective therapy within 14 days prior to the first dose, history of pneumonitis or interstitial lung disease, patients with active brain metastases, history of significant cardiovascular disease, a history of hypersensitivity to another monoclonal antibody, systemic immunosuppressive medicinal products within 2 weeks prior to study entry.

Interaction with Other Medicinal Products and Other Forms of Interaction
Serplulimab is a humanized monoclonal antibody, as such pharmacokinetic drug-drug interaction studies have not been conducted. As monoclonal antibodies are not metabolised by cytochrome P450 (CYP) enzymes or other drug metabolising enzymes, inhibition, or induction of these enzymes by co-administered medicinal products is not anticipated to affect the pharmacokinetics of serplulimab.
The use of systemic corticosteroids or immunosuppressants before starting serplulimab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of serplulimab. However, systemic corticosteroids or other immunosuppressants can be used to treat immune-related adverse reactions after starting serplulimab (see section **Special Warnings and Precautions for Use).**

Fertility, Pregnancy and Lactation
Pregnancy
There is no data on the use of Zerpidio in pregnant women. Animal studies have demonstrated that inhibition of the PD-1 pathway has embryofoetal toxicity. Human IgG is known to cross the placental barrier and serplulimab is an IgG4; therefore, serplulimab has the potential to be transmitted from the mother to the developing foetus. Serplulimab is not recommended during pregnancy unless the clinical benefit outweighs the potential risk.

Breast-feeding
It is unknown whether serplulimab is secreted in human milk and the effect on the production of breast milk. Since it is known that human IgG antibodies can be secreted in breast milk, a risk to the breast-fed newborns/infants cannot be excluded. Therefore, it is recommended that lactating women should stop breast-feeding for the child during treatment with serplulimab and for at least 6 months after the last dose of serplulimab.

Fertility
Studies to evaluate the effect of serplulimab on fertility have not been performed.Thus, the effect of Zerpidio on male and female fertility is unknown.

Contraception
Women of childbearing potential should use effective contraceptive during treatment with serplulimab and for at least 6 months after the last dose of serplulimab.

Effects on Ability to Drive and Use Machines
Serplulimab may have a minor influence on the ability to drive and use machines. Because of potential adverse reactions such as fatigue (see section **Undesirable Effects**), patients should be advised to use caution when driving or operating machinery until they are certain that serplulimab does not adversely affect them.

Undesirable Effects
Summary of the safety profile
The safety of Zerpidio was evaluated in HLX10-005-SCLC301, a randomised (2:1), double-blind, multiregional clinical trial in 585 patients with previously untreated ES-SCLC. Patients received Zerpidio 4.5 mg/kg every 3 weeks in combination with carboplatin and etoposide (n=389), or placebo in combination with carboplatin and etoposide (n=196) every 3 weeks. The most common adverse reactions (≥ 20%) were neutropenia (25.7%), leukopenia (24.7%), and anaemia (22.1%).
Tabulated summary of adverse reactions
Adverse reactions observed in patients who received Zerpidio in combination with carboplatin and etoposide in HLX10-005-SCLC301 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); very rare (< 1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 3. Adverse reactions in patients treated with Zerpidio* in HLX10-005-SCLC301

Zerpidio with carboplatin and etoposide	
Blood and lymphatic system disorders	
Very common	Neutropenia[a], leukopenia[b], anaemia[c], thrombocytopenia[d]
Common	lymphopenia[e]
Uncommon	platelet count increased, granulocytopenia[f], neutrophilia[g], white blood cell count increased, lymphadenitis, myelosuppression
Metabolism and nutrition disorders	
Very common	hyperlipidaemia[h], decreased appetite
Common	hypoproteinaemia[i], hyponatraemia, hypokalaemia, hypocalcaemia [j], hypomagnesaemia,hyperuricaemia[k], hypochloraemia, hyperphosphataemia, hypophosphataemia.
Uncommon	hyperkalaemia[l], hypermagnesaemia , hypoglycaemia, hypercalcaemia.
Gastrointestinal disorders	
Very common	nausea
Common	vomiting, constipation, diarrhoea, abdominal pain[m], dysphagia, flatulence[n], gastrointestinal disorder [o]
Uncommon	dry mouth, gastrooesophageal reflux disease[p], mouth ulceration[q], stomatitis, enteritis, gastritis, burn oral cavity, immune-mediated pancreatitis, dyspepsia, gingival bleeding.
Endocrine disorders	
Very common	hypothyroidism[r], hyperthyroidism
Common	hyperglycaemia or diabetes mellitus[s], thyroiditis[t]
Uncommon	adrenal insufficiency[u], thyroid disorders[v], hyperadrenocorticism[w], hypophysitis.
Skin and subcutaneous tissue disorders	
Common	Rash[x], alopecia, pruritus, dermatitis[y]
Uncommon	pigmentation disorder[z], hyperhidrosis, psoriasis, dry skin.
General disorders and administration site conditions	
Common	pyrexia[aa], asthenia[bb], fatigue, malaise, edema[cc]
Uncommon	chills
Cardiac disorders	
Common	arrhythmia[dd], sinus tachycardia[ee], conduction defects[ff], sinus bradycardia, cardiac failure[gg]
Uncommon	cardiomyopathy[hh], myocardial ischaemia, pericardial effusion
Hepatobiliary disorders	
Common	hyperbilirubinaemia [ii], liver injury[jj]
Respiratory, thoracic, and mediastinal disorders	
Common	pneumonitis[kk], chest discomfort[ll], dyspnoea[mm], cough[nn]
Uncommon	oropharyngeal pain, pneumothorax
Infections and infestations	
Common	pneumonia[oo], urinary tract infection[pp], upper respiratory tract infection[qq]
Uncommon	septic shock, skin infection, enteritis infection, lip infection, meningoencephalitis herpetic, chalazion
Renal and urinary disorders	
Common	protein urine present[rr], haematuria[ss], renal injury[tt]
Uncommon	glycosuria, white blood cells urine positive
Nervous system disorders	
Common	paraesthesia[uu], dizziness, headache
Uncommon	immune-mediated encephalitis[vv], neuropathy peripheral[ww], hypersomnia[xx], motion sickness, neurotoxicity, cognitive disorder, memory impairment, motor dysfunction, tremor
Musculoskeletal and connective tissue disorders	
Common	musculoskeletal pain[yy], arthralgia, pain in extremity
Uncommon	arthritis[zz], musculoskeletal discomfort[aaa], autoimmune myositis
Psychiatric disorders	
Common	insomnia[bbb]
Vascular disorders	
Common	hypertension
Uncommon	hypotension, vasculitis[ccc]
Immune system disorders	
Common	infusion-related reaction[ddd]
Eye disorders	
Uncommon	vision blurred
Social circumstances	
Uncommon	loss of personal independence in daily activities
Investigations	
Very common	alanine aminotransferase increased
Common	aspartate aminotransferase increased, blood alkaline phosphatase increased, gamma-glutamyltransferase increased, blood lactate dehydrogenase increased, weight decreased, electrocardiogram abnormal[eee], blood urea increased, thyroid function test abnormal [fff], myoglobin blood increased, blood creatine phosphokinase increased [ggg], coagulation function test abnormal [hhh], troponin increased[iii], blood creatinine increased
Uncommon	n-terminal prohormone brain natriuretic peptide increased, lipoprotein abnormal[jjj], myocardial necrosis marker increased, monocyte count increased, transaminases increased

*Adverse Reaction frequencies presented in Table 3 may not be fully attributeable to Zerpidio alone but may contain contributions from the underlying disease or from other medicinal products used in a combination
The following terms represent a group of related events that describe a medical condition rather than a single event:

a. Includes neutrophil count decreased, neutropenia, febrile neutropenia
b. Includes white blood cell count decreased, leukopenia
c. Includes anaemia, haemoglobin decreased, red blood cell count decreased
d. Includes platelet count decreased, thrombocytopenia
e. Includes lymphocyte count decreased, lymphopenia
f. Includes granulocyte count decreased, granulocytopenia
g. Includes neutrophil count increased, neutrophilia
h. Includes hypercholesterolaemia, hypertriglyceridaemia, blood cholesterol increased, hyperlipidaemia
i. Includes hypoalbuminaemia, hypoproteinaemia
j. Includes hypocalcaemia, blood calcium decreased
k. Includes hyperuricaemia, blood uric acid increased
l. Includes hyperkalaemia, blood potassium increased.
m. Includes abdominal pain upper, abdominal discomfort, abdominal pain, abdominal pain lower.
n. Includes abdominal distension, flatulence.
o. Includes gastrointestinal haemorrhage, gastrointestinal disorder, lower gastrointestinal haemorrhage.
p. Includes gastrooesophageal reflux disease, regurgitation.
q. Includes aphthous ulcer, mouth ulceration.
r. Includes hypothyroidism, blood thyroid stimulating hormone increased, thyroxine free decreased, central hypothyroidism, tri-iodothyronine decreased.
s. Includes hyperglycaemia, diabetes mellitus, diabetic ketoacidosis, blood ketone body increased, glucose tolerance impaired, ketoacidosis.
t. Includes thyroid disorder, thyroiditis.
u. Includes adrenal insufficiency, cortisol decreased.
v. Includes euthyroid sick syndrome, ultrasound thyroid abnormal.
w. Includes cortisol increased, hyperadrenocorticism.
x. Includes rash, rash maculo-papular, eczema, drug eruption, erythema, skin toxicity.
y. Includes autoimmune dermatitis, dermatitis, dermatitis allergic, dermatitis bullous, seborrhoeic dermatitis.
z. Includes skin hyperpigmentation, vitiligo.
aa. Includes pyrexia, body temperature increased.
bb. Includes asthenia, general physical health deterioration.
cc. Includes face oedema, oedema peripheral, peripheral swelling, swelling, swelling face.
dd. Includes supraventricular extrasystoles, supraventricular tachycardia, arrhythmia, ventricular extrasystoles, arrhythmia supraventricular, atrial fibrillation, atrial tachycardia, bradyarrhythmia, early repolarisation syndrome, ventricular arrhythmia.
ee. Includes sinus tachycardia, tachycardia
ff. Includes atrioventricular block first degree, bundle branch block right, atrial conduction time prolongation, bundle branch block left, defect conduction intraventricular.
gg. Includes cardiac failure, cardiac failure acute, left ventricular failure.
hh. Includes cardiomyopathy, metabolic cardiomyopathy.
ii. Includes blood bilirubin increased, bilirubin conjugated increased, hyperbilirubinaemia, blood bilirubin unconjugated increased.
jj. Includes hepatic function abnormal, drug-induced liver injury, liver injury, immune-mediated hepatitis.
kk. Includes immune-mediated lung disease, pneumonitis, interstitial lung disease.
ll. Includes chest discomfort, non-cardiac chest pain, chest pain.
mm. Includes dyspnoea, asphyxia.
nn. Includes cough, productive cough.
oo. Includes pneumonia, pneumonia fungal
pp. Includes urinary tract infection, asymptomatic bacteriuria.
qq. Includes upper respiratory tract infection, pharyngotonsillitis, tonsillitis.
rr. Includes proteinuria, protein urine present, albuminuria.
ss. Includes haematuria, urinary occult blood positive.
tt. Includes acute kidney injury, renal failure, renal impairment, renal injury.
uu. Includes paraesthesia, hypoaesthesia.
vv. Includes immune-mediated encephalitis, encephalitis autoimmune
ww. Includes neuropathy peripheral, peripheral sensorimotor neuropathy
xx. Includes hypersomnia, somnolence.
yy. Includes back pain, myalgia, musculoskeletal chest pain, spinal pain.
zz. Includes arthritis, joint effusion.
aaa. Includes muscular weakness, musculoskeletal discomfort.
bbb. Includes insomnia, poor quality sleep.
ccc. Includes phlebitis, phlebitis superficial
ddd. Includes drug hypersensitivity, anaphylactic reaction, infusion related reaction
eee. Includes electrocardiogram QT prolonged, electrocardiogram repolarisation abnormality, electrocardiogram T wave abnormal
fff. Includes blood thyroid stimulating hormone decreased, tri-iodothyronine increased, anti-thyroid antibody positive, thyroglobulin increased, thyroxine increased.
ggg. Includes blood creatine phosphokinase increased, blood creatine phosphokinase MB increased
hhh. Includes activated partial thromboplastin time prolonged, activated partial thromboplastin time shortened, international normalised ratio decreased, prothrombin level increased.
iii. Includes troponin increased, troponin I increased, troponin T increased.
jjj. Includes lipoprotein increased, low density lipoprotein increased.

Description of selected adverse reactions
Zerpidio is associated with immune-related adverse reactions. The data for the following immune-related adverse reactions are based on 1172 patients who received Zerpidio monotherapy (n=263) or in combination with other medicinal products (n=909) across eight doses (0.3, 1, 3, 10 mg/kg every 2 weeks, 4.5 mg/kg every 3 weeks, 200 mg every 2 weeks, 300 mg every 3 weeks, or 400 mg every 4 weeks) in eight clinical studies. The management guidelines for these adverse reactions are described in section**s Posology and Method of Administration and Special Warnings** and **Precautions for Use.**
Immune-related lung disease
Immune-related lung disease occurred in 41 (3.5%) patients, including Grade 3 in 11 (0.9%) patients, Grade 4 in 1 (0.1%) patient and Grade 5 in 3 (0.3%) patients. The median time to onset was 2.79 months (range: 0.03-23.33 months). The median duration was 1.74 months (range: 0.13-13.34 months). 19 (1.6%) patients received high-dose corticosteroid treatment. Immune-related lung disease led to discontinuation of serplulimab in 12 (1.0%) patients. Resolution occurred in 8 patients.

Immune-related colitis
Immune-related colitis occurred in 27 (2.3%) patients, including Grade 3 in 5 (0.4%) patients and Grade 5 in 1 (0.1%) patient. The time to onset was 2.83 months (range: 0.03-7.95 months). The median duration was 0.43 months (range: 0.03-4.07 months). 5 (0.4%) patients received high-dose corticosteroid treatment. Immune-related colitis led to discontinuation of serplulimab in 4 (0.3%) patients. Resolution occurred in 16 patients.

Immune-related hepatitis
Hepatitis occurred in 9 (0.8%) patients, including Grade 3 in 4 (0.3%) patients, Grade 4 in 2 (0.2%) patients and Grade 5 in 2 (0.2%) patients. The median time to onset was 2.76 months (range: 0.43-6.60 months). The median duration was 1.05 months (range: 0.53-1.51 months). 2 (0.2%) patients received high-dose corticosteroid treatment. Hepatitis led to discontinuation of serplulimab in 4 (0.3%) patients. Resolution occurred in 3 patients. Abnormal liver function occurred in 51 (4.4%) patients, including Grade 3 in 10 (0.9%) patients. The median time to onset was 1.41 months (range: 0.07-29.73 months). The median duration was 1.40 months (range: 0.26-13.80 months). 3 (0.3%) patients received high-dose corticosteroid treatment. Abnormal liver function led to discontinuation of serplulimab in 3 (0.3%) patients. Resolution occurred in 20 patients.

Immune-related nephritis and renal dysfunction
Immune-related nephritis and renal dysfunction occurred in 28 (2.4%) patients, including Grade 3 in 3 (0.3%) patients and Grade 4 in 1 (0.1%) patient. The median time to onset was 2.78 months (range: 0.23-17.28 months). The median duration was 1.12 months (range: 0.13-5.32 months). 2 (0.2%) patients received high-dose corticosteroid treatment. Immune-related nephritis and renal dysfunction led to discontinuation of serplulimab in 2 (0.2%) patients. Resolution occurred in 12 patients.

Immune-related endocrinopathies
Hypothyroidism
Hypothyroidism occurred in 123 (10.5%) patients, including Grade 3 in 1 (0.1%) patient. The median time to onset was 3.71 months (range: 0.62-14.46 months). The median duration was 2.89 months (range: 0.69-7.49 months). 66 (5.6%) patients received thyroid hormone replacement therapy. No patients discontinued serplulimab due to hypothyroidism. Resolution occurred in 29 patients.

Hyperthyroidism
Hyperthyroidism occurred in 72 (6.1%) patients, and there were no Grade ≥3 hyperthyroidism. The median time to onset was 1.77 months (range: 0.69-26.84 months). The median duration was 1.41 months (range: 0.07-2.83 months). 1 (0.1%) patient received thyroid hormone replacement therapy. No patients discontinued serplulimab due to hyperthyroidism. Resolution occurred in 46 patients.

Thyroiditis
Thyroiditis occurred in 8 (0.7%) patients, and there were no Grade ≥ 3 thyroiditis. The median time to onset was 5.65 months (range: 1.94-13.50 months). The duration was 0.56 months. 2 (0.2%) patients received thyroid hormone replacement therapy. No patients discontinued serplulimab due to thyroiditis. Resolution occurred in 1 patient.

Adrenal gland disorders
Adrenal gland disorders occurred in 4 (0.3%) patients, including Grade 3 in 1 (0.1%) patient. The median time to onset was 5.77 months (range: 4.04-6.93 months). The median duration was not reached. 1 (0.1%) patient received high-dose corticosteroid treatment. No patients discontinued Zerpidio due to adrenal gland disorders.

Pituitary disorders
Pituitary disorders occurred in 9 (0.8%) patients, including Grade 3 in 1 (0.1%) patient. The median time to onset was 6.97 months (range: 1.41-11.50 months). The median duration was 2.43 months. 1 (0.1%) patient received thyroid hormone replacement therapy. Pituitary disorders led to discontinuation of Zerpidio in 2 (0.2%) patients.

Diabetes mellitus/hyperglycemia
Diabetes mellitus/hyperglycaemia occurred in 12 (1.0%) patients, including Grade 3 in 6 (0.5%) patients and Grade 4 in 1 (0.1%) patient. The median time to onset was 4.09 months (range: 0.69-11.10 months), The median duration was 3.63 months (range: 2.96-4.30 months). 6 (0.5%) patients received insulin replacement therapy. Diabetes mellitus/hyperglycaemia led to discontinuation of serplulimab in 1 (0.1%) patient.

Immune-related skin adverse reactions
Immune-related skin adverse reactions occurred in 97 (8.3%) patients, including Grade 3 in 8 (0.7%) patients. The median time to onset was 1.74 months (range: 0.03-15.77 months). The median duration was 0.79 months (range: 0.07-10.91 months). 15 (1.3%) patients received high-dose corticosteroid treatment. Immune-related skin adverse reactions led to discontinuation of serplulimab in 5 (0.4%) patients. Resolution occurred in 53 patients.

Immune-related pancreatitis
Immune-related pancreatitis occurred in 13 (1.1%) patients, including Grade 3 in 4 (0.3%) patients, Grade 4 in 1 (0.1%) patient and Grade 5 in 1 (0.1%) patient. The median time to onset was 2.30 months (range: 0.23-12.42 months). The median duration was 0.72 months (range: 0.16-4.14 months). 2 (0.2%) patients received high-dose corticosteroid treatment. Immune-related pancreatitis led to discontinuation of serplulimab in 2 (0.2%) patients. Resolution occurred in 4 patients.

Immune-related myocarditis
Immune-related myocarditis occurred in 6 (0.5%) patients, including Grade 3 in 2 (0.2%) patients and Grade 5 in 1 (0.1%) patient. The median time to onset was 1.68 months (range: 0.26-25.36 months). The median duration was 1.02 months (range: 0.76-4.57 months). 3 (0.3%) patients received high-dose corticosteroid treatment. Immune-related myocarditis led to discontinuation of ZERPIDIO in 1 (0.1%) patient. Resolution occurred in 1 patient.

Immune-related uveitis
Immune-related uveitis occurred in 1 (0.1%) patient, which was Grade 1. The time to onset was 6.90 months. The duration of immune-related uveitis was 1.35 months. The event resolved for the patient.

Other immune-related adverse reactions
The other clinically significant immune-related adverse reactions reported in patients who received Zerpidio were as follows. Severe or fatal cases have been reported for some of these adverse reactions.

Cardiac/Vascular: Sinus bradycardia, ventricular extrasystoles, arrhythmia, supraventricular extrasystoles, acute coronary syndrome, acute myocardial infarction, atrial flutter, atrioventricular block first degree, cardiac failure acute, cardiotoxicity, extrasystoles, myocardial infarction, sinus arrhythmia, sinus tachycardia, tachycardia, capillary disorder, hypertension, hypotension.

Nervous system: Dizziness, immune-mediated encephalitis, neuropathy peripheral, encephalitis autoimmune, encephalopathy, facial paralysis, neuralgia, neurotoxicity, peripheral sensorimotor neuropathy, post herpetic neuralgia.

Gastrointestinal: Nausea, abdominal distension, vomiting, mouth ulceration, abdominal discomfort, abdominal pain, abdominal pain upper, dry mouth, gastrointestinal pain, gingival pain, oral lichen planus, stomatitis, toothache.

Musculoskeletal and connective tissue: Arthralgia, muscular weakness, back pain, myalgia, pain in extremity, autoimmune myositis, joint effusion, joint swelling.

Metabolism and nutrition: Decreased appetite, hypokalaemia, hyperlipidaemia, hypertriglyceridaemia, hyperuricaemia, hypoalbuminaemia, hypochloraemia, hyponatraemia, electrolyte imbalance, hypercholesterolaemia, hypomagnesaemia, hypophosphataemia, hypozincaemia, iron deficiency.

General disorders and administration site conditions: Malaise, asthenia, fatigue, pyrexia, chills, face oedema, non-cardiac chest pain, oedema peripheral, pain, peripheral swelling, swelling.

Respiratory, thoracic and mediastinal: Dyspnoea, chronic obstructive pulmonary disease, cough, dysphonia, pleural effusion, respiratory failure.

Infections and infestations: Herpes zoster, rash pustular, sepsis, hepatitis B reactivation, skin infection, urethritis, urinary tract infection.

Endocrine: Euthyroid sick syndrome, goitre, hyperadrenocorticism, primary hyperaldosteronism.

Other (Blood and lymphatic system/Psychiatric/Ear and labyrinth/Eye/Hepatobiliary/Reproductive system and breast): Anaemia, leukopenia, thrombocytopenia, immune thrombocytopenia, neutropenia, insomnia, panic disorder, motion sickness, tinnitus, vision blurred, cholangitis acute, drug-induced liver injury, menstrual disorder.

Infusion-related reactions
Infusion-related reactions occurred in 14 (1.2%) patients, including Grade 3 in 2 (0.2%) patients and Grade 4 in 1 (0.1%) patient. The median time to onset was 0.90 months (range: 0.03-8.57 months). The median duration was 0.07 months (range: 0.03-0.53 months). No patients discontinued Zerpidio due to infusion related reactions. Resolution occurred in 13 patients.

Immune-related laboratory abnormalities
The proportion of patients who experienced a shift from baseline to a Grade ≥ 3 laboratory abnormality was as follows: 0.4% for platelet count decreased, 0.4% for neutrophil count decreased, 0.2% for white blood cell count decreased, 0.2% for blood creatine phosphokinase increased, 0.1% for blood lactate dehydrogenase increased, 0.1% for blood cholesterol increased.

Immunogenicity
The immunogenicity of serplulimab was evaluated in 1172 patients who were treated with serplulimab 0.3, 1, 3, 10 mg/kg every 2 weeks, 4.5 mg/kg every 3 weeks, 200 mg every 2 weeks, 300 mg every 3 weeks, or 400 mg every 4 weeks. 40 (3.4%) patients tested positive for treatment-emergent antibodies to serplulimab. No patients had neutralising antibodies (NAb) against serplulimab. There was no evidence of an altered pharmacokinetics or safety profile with anti-serplulimab binding or neutralising antibody development.

Paediatric population
The safety of Zerpidio in children and adolescents have not been established. No data is available.

Elderly
The safety analysis demonstrated treatment-emergent adverse events (TEAEs) of grade 3 or higher in 64.4% of patients under 65 years of age and in 73.4% of patients aged 65 years or older. Treatment-emergent serious adverse events (SAEs) occurred in 34.6% of patients under 65 years and in 43.7% of patients aged 65 years or older. TEAEs leading to death were observed in 9.5% of patients under 65 years and in 11.8% of patients aged 65 years or older.

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.

Overdose
There is no information on overdose with serplulimab. In case of overdose, patients must be closely monitored for signs or symptoms of adverse reactions, and appropriate symptomatic treatment instituted immediately.

Special Precautions for Storage
Store in a refrigerator (2 – 8 °C). Do not freeze. Do not shake.
Keep the vial in the outer carton in order to protect from light.

Packaging
Box, 1 vial @ 10 ml

Nature and contents of container
Injection vials are made of middle borosilicate Ph. Eur. Type I glass tubing and chlorobutyl rubber stoppers for injectable drug.

KEEP OUT OF REACH OF CHILDREN
ON MEDICAL PRESCRIPTION ONLY

Reg No.:

Manufactured by:
Shanghai Henlius Biopharmaceutical Co., Ltd
(Building D) Block 1, No. 1289 Yishan Road, Xuhui district, Shanghai, PRC

Product Registrant:
Innogene Kalbiotech Pte. Ltd., Singapore

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