

Chemotherapy Protocol

LUNG CANCER– SMALL CELL (SCLC)

SERPLULIMAB-CARBOPLATIN (AUC5)-ETOPOSIDE(IV/PO)

Regimen

- Lung - Serplulimab-Carboplatin (AUC5)-Etoposide(IV/PO)

Indication

- First-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC)
- WHO performance status 0 or 1

Toxicity

Drug	Adverse Effect
Serplulimab	Neutropenia, leukopenia, anaemia, thrombocytopenia, hyperlipidaemia, hypoproteinemia, hyponatraemia, pneumonitis, hyperglycaemia, diabetes mellitus, hypothyroidism, hyperthyroidism, immune related skin AEs, hepatitis, fatigue, colitis
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances
Etoposide	Hypotension on rapid infusion, alopecia, hyperbilirubinaemia

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs (including albumin), U&Es, glucose and cortisol prior to day one each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- Thyroid function tests prior to starting Serplulimab treatment and then every 6 weeks or when clinically indicated

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Prior to prescribing on day one of cycles 1 – 4 the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

If neutrophils are less than 1.5 or platelets less than 100 delay treatment for 1 week. Repeat FBC and, if within or normal parameters, resume treatment at full dose.

If the counts do not recover within 7 days or repeated delays are required consider reduction of oral etoposide dose to $100\text{mg}/\text{m}^2$ on Day 2 and Day 3.

Consider blood transfusion if patient symptomatic of anaemia or haemoglobin of less than $8\text{g}/\text{dL}$ ($80\text{g}/\text{L}$).

There are no standard dose adjustments for haematological toxicity with serplulimab toxicity.

Hepatic Impairment

Drug	Bilirubin ($\mu\text{mol}/\text{L}$)		AST/ALT units	Dose
Serplulimab	1.5-3xULN	OR	3-5xULN	Insufficient data, clinical decision
	Greater than 3xULN	OR	Greater than 3xULN	
Carboplatin	N/A		N/A	No dose adjustment needed
Etoposide	26-51	or	60-180	50%
	more than 51	or	more than 180	clinical decision

For patients with pre-existing mild hepatic impairment no dose adjustment is recommended. Serplulimab has not been studied in patients with moderate or severe hepatic impairment.

For a NCI-CTC grade 2 hepatitis (ALT or AST between 3-5xULN or bilirubin between 1.5-3xULN) that persists for between 5-7 days then withhold the serplulimab and consider treatment with a corticosteroid. The corticosteroid may be resumed when the event improves to grade 1 or below within 12 weeks and the corticosteroid dose has been reduced to the equivalent of oral prednisolone 10mg per day or less.

For a grade 3 or above hepatitis (ALT or AST greater than 5xULN or bilirubin greater than 3xULN) permanently discontinue serplulimab

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose
Serplulimab	≥30	No dose adjustment needed
	<30	Insufficient data (not recommended)
Carboplatin*	less than 20	Omit
Etoposide	more than 50	100%
	15-50	75%
	less than 15	50%

* Significant changes in GFR of more than 10% may require dose adjustment.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Serplulimab

Serplulimab belongs to the immunotherapy class of cancer treatments. Autoimmune toxicities are most frequently noted and can be life threatening. If autoimmune toxicities occur delaying treatment should be considered while investigations or treatments are organised. Some, but not all, toxicities mandate cessation of treatment. Please seek guidance from relevant site-specific specialist teams or oncologists / haematologists with experience of prescribing these agents. Clinicians should be aware that the current funding approval precludes further treatment after an interruption of 12 weeks or longer; this situation may change.

Refer to the latest version of the European Society of Medical Oncology guidelines; Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up ⁽³⁾.

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Immune-related adverse reactions, which can be severe or life-threatening, may involve the gastrointestinal, liver, skin, nervous, endocrine, or other organ systems. Most occur during treatment, however, onset months after the last dose has been reported. Unless an alternate aetiology has been identified, diarrhoea, increased stool frequency, bloody stool, LFT elevations, rash and endocrinopathy must be considered inflammatory and serplulimab-related. Early diagnosis and appropriate management are essential to minimise life-threatening complications.

Serplulimab should be permanently discontinued for: any NCI-CTC grade 3 or 4 pneumonitis or hepatitis; any other life-threatening NCI-CTC grade 4 reaction (including colitis and renal impairment); any recurrence of a severe or NCI-CTC grade 3 reaction; any persistent NCI-CTC grade 2 or 3 treatment-related adverse reaction that does not recover to grade 1 or resolve within 12 weeks after the last dose.

Immune-related adverse reaction	Severity	Treatment modification
Immune-related pneumonitis	Grade 2 pneumonitis	Withhold until symptoms resolve and radiographic abnormalities improve. Consider treatment with oral prednisolone 1-2mg/kg or equivalent per day Treatment may be resumed if the event improves to grade 0 or grade 1 within 12 weeks, and corticosteroids have been reduced to 10mg or less oral prednisone equivalent per day.
	Grade 3 or 4 pneumonitis	Permanently discontinue serplulimab. Consider treatment with corticosteroids.
Immune-related colitis	Grade 2 or 3 diarrhoea or symptomatic colitis	Withhold serplulimab initially. For a grade 2 diarrhoea or colitis, if the symptoms persist for more than 5 days or recur, start treatment with 1-2mg/kg oral prednisolone or equivalent per day For a grade 3 diarrhoea or colitis treatment with intravenous corticosteroids should be started, this may be converted to oral treatment as symptoms improve. If the symptoms improve to grade 1 or less taper the corticosteroids over one month Treatment may be resumed if the event improves to grade 0 or grade 1 within 12 weeks, and corticosteroids have been reduced to 10mg or less oral prednisone equivalent per day
	Grade 4 diarrhoea or colitis	Permanently discontinue serplulimab. Consider treatment with corticosteroids.
Immune-related pancreatitis	Grade 3 or 4 serum amylase or lipase levels increased (more than 2xULN) or grade 2 or 3 pancreatitis	Withhold serplulimab Treatment with serplulimab may be resumed if serum amylase and lipase levels improve to grade 0 or grade 1 within 12 weeks, or symptoms of pancreatitis have resolved, and corticosteroids have been reduced to 10mg or less oral prednisone or equivalent per day
	Grade 4 or recurrent pancreatitis	Permanently discontinue serplulimab. Consider treatment with corticosteroids.

Immune-related thyroid disorders	Symptomatic	Withhold serplulimab <i>Hypothyroidism</i> Treatment may be resumed when symptoms are controlled by thyroid replacement therapy and TSH levels are decreasing <i>Hyperthyroidism</i> Treatment may be resumed when symptoms are controlled by cabimazole or equivalent and thyroid function is improving
Immune-related adrenal insufficiency	Symptomatic	Withhold serplulimab Treatment may be resumed if the symptoms improve to grade 0 or grade 1 within 12 weeks and corticosteroids have been reduced to the equivalent of 10mg or less of oral prednisone or equivalent per day and patient is stable on replacement therapy
Immune-related diabetes mellitus	Grade 3 or 4 hyperglycaemia (fasting glucose more than 250-500mg/dL)	Withhold serplulimab Treatment may be resumed if metabolic control is achieved on insulin replacement therapy
Immune-related myasthenic syndrome / myasthenia gravis, Guillain-Barre syndrome and meningoencephalitis	All grades	Permanently discontinue serplulimab
Myositis	Grade 2-3	Withhold for a moderate to severe myositis and discontinue
	Grade 3-4	Permanently discontinue
Infusion related reactions	Grade 1	Reduce the infusion rate to half Once the event has resolved, wait for 30minutes while delivering the infusion at the reduced rate. If tolerated, the infusion rate may then be increased to original rate
	Grade 2	Withhold serplulimab Restart at half of the infusion rate only after the symptoms have resolved
	Grade 4	Permanently discontinue serplulimab
Immune-related rash	Grade 3 rash	Withhold serplulimab Treatment may be resumed if the rash is resolved and corticosteroids have been reduced to 10mg or less oral prednisone equivalent per day
	Grade 4 rash	Permanently discontinue serplulimab. Consider treatment with corticosteroids

Etoposide

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

Regimen

A total of 12 cycles will be set in ARIA

Induction - 21 day cycle for 4 cycles

Drug	Dose	Days	Administration
Serplulimab	4.5mg/kg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 100mL/hour *
Carboplatin	AUC 5 (maximum dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Etoposide	100mg/m ²	1	Intravenous infusion in 1000ml sodium chloride 0.9%
Etoposide	200mg/m ²	2,3	Oral

Followed by:

Maintenance – 21 day cycle until disease progression or unacceptable toxicity

Drug	Dose	Days	Administration
Serplulimab	4.5mg/kg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30min *

* The initial serplulimab infusion rate should be set up to 100mL per hour. If the first infusion is well tolerated, all subsequent infusions may be given over 30 minutes (+/- 10 minutes). The infusion rate can be adjusted if infusion-related reactions occur.

Dose Information

- The recommended maximum dose when using a calculated creatinine clearance at AUC 5 is 750mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant. In ARIA the maximum dose has been set at 790mg to comply with the national dose bands. Please check this maximum dose is suitable for you patient.
- It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.
- Carboplatin dose will be dose banded in accordance with the national dose bands (10mg/ml).
- Intravenous etoposide will be dose banded in accordance with the national dose bands (20mg/ml)
- Oral etoposide is available as 50mg and 100mg soft capsules.

[Administration Information](#)

[Extravasation](#)

- Serplulimab – neutral
- Carboplatin – irritant
- Etoposide – irritant

[Other](#)

- The first infusion of serplulimab should be set at a rate of 100mL per hour. If this is well tolerated subsequent infusions can be administered over 30minutes. The infusion rate can be adjusted if infusion-related reactions occur.

[Additional Therapy](#)

- Antiemetics (Cycles 1-4 Day 1 only)

15-30 minutes prior to chemotherapy

- ondansetron 8mg oral or intravenous

As take home medication

- dexamethasone 4mg oral twice a day for 3 days
- metoclopramide 10mg oral three times a day as required
- ondansetron 8mg oral twice a day for 3 days

- Growth factor as per local formulary choice (Cycles 1-4 only), for example:

- filgrastim or bioequivalent 30million units once a day for 5 days starting on day 5 of the cycle subcutaneous
- lenograstim or bioequivalent 33.6million units once a day for 5 days starting on day 5 of the cycle subcutaneous
- Pegfilgrastim, lipegfilgrastim or bioequivalent 6mg on the day after SACT administration

- As required for the treatment of infusion related reactions;

- chlorphenamine 10mg intravenous
- hydrocortisone 100mg intravenous
- paracetamol 1000mg oral

- Loperamide 4mg oral initially followed by 2mg after each loose stool when required for the relief of diarrhoea (maximum 16mg/24 hours).
- Gastric protection with a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed

Additional Information

- The use of systemic corticosteroids, before starting treatment with serplulimab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of the agent. However, systemic corticosteroids can be used after starting serplulimab to treat immune-related adverse reactions.
- Patients must be given a Serplulimab immunotherapy Patient Alert Card.
- Oral etoposide capsules should be swallowed whole on an empty stomach or an hour before food.

References

1. Hetronify® 10 mg/ml concentrate for solution for infusion Summary of Product Characteristics. Accord Healthcare Ltd.
2. NICE national Institute for Health and Care Excellence, Serplulimab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer: final draft guidance TA11405, June 2026
3. Accord-UK Ltd, Hetronify® Formulary Application Support Pack, October 2025
4. Cheng Y, Zhang S, Han L, et al. First-line serplulimab plus chemotherapy in extensive-stage small-cell lung cancer: Updated results and biomarker analysis from the ASTRUM-005 randomized clinical trial. Cancer Commun (Lond). Published online May 29, 2025. doi:10.1002/cac2.70032.

REGIMEN SUMMARY

Serplulimab-Carboplatin (AUC5)-Etoposide(IV/PO)

Cycle 1 Day 1

1. Serplulimab 4.5mg/kg intravenous infusion in 100ml sodium chloride 0.9% over 100ml/hour
Administration Instructions
Administer the infusion solution intravenously using a sterile, non-pyrogenic, low-protein binding 0.2 to 5.0 µm in-line or add-on filter.
The first infusion should be administered over 100ml/hour. If this is well tolerated subsequent infusions can be administered over 30minutes.
Ensure the patient has been given a serplulimab patient alert card.
2. Ondansetron 8mg oral or intravenous
Administration Instructions
Administer 15-30 minutes prior to chemotherapy. This may be given as ondansetron 8mg IV stat if required.
3. Carboplatin AUC 5 (maximum dose) intravenous infusion in 500ml glucose 5% over 60 minutes
Administration Instructions
The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient.
4. Etoposide 100mg/m² intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
5. Chlorphenamine 10mg intravenous injection when required for infusion related reactions
6. Hydrocortisone 100mg intravenous injection when required for infusion related reactions
7. Paracetamol 1000mg oral when required for infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines (Day 1 only)

8. Etoposide 200mg/m² oral once a day on days 2 and 3
9. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy
10. Metoclopramide 10mg oral three times a day for three days then 10mg three times a day when required for nausea
11. Ondansetron 8mg oral twice a day for 3 days starting on the evening of day one or treatment
Administration Instructions
Start on the evening of day 1 of the treatment cycle
12. Growth Factor as directed
Administration instructions
Growth factor as per local formulary choice. For example;
filgrastim or bioequivalent 30million units once a day for 5 days starting on day 5 of the cycle subcutaneous
lenograstim or bioequivalent 33.6million units once a day for 5 days starting on day 5 of the cycle subcutaneous
Pegfilgrastim or lipegfilgrastim or bioequivalent 6mg on the day after SACT administration
13. Loperamide as directed (cycle 1 only)
Administration Instructions

Take 4mg after the first loose stool and then 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours.
Please supply one original pack size

Cycle 2, 3, 4 Day 1

14. Serplulimab 4.5mg/kg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Administration Instructions

Administer the infusion solution intravenously using a sterile, non-pyrogenic, low-protein binding 0.2 to 5.0 µm in-line or add-on filter.

The first infusion should be administered over 100ml/hour. If this is well tolerated subsequent infusions can be administered over 30minutes.

Ensure the patient has been given a serplulimab patient alert card.

15. Ondansetron 8mg oral or intravenous

Administration Instructions

Administer 15-30 minutes prior to chemotherapy. This may be given as ondansetron 8mg IV stat if required.

16. Carboplatin AUC 5 (maximum dose) intravenous infusion in 500ml glucose 5% over 60 minutes

Administration Instructions

The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient.

17. Etoposide 100mg/m² intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

18. Chlorphenamine 10mg intravenous injection when required for infusion related reactions

19. Hydrocortisone 100mg intravenous injection when required for infusion related reactions

20. Paracetamol 1000mg oral when required for infusion related reactions

Administration Instructions

Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines (Day 1 only)

21. Etoposide 200mg/m² oral once a day on days 2 and 3

22. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy

23. Metoclopramide 10mg oral three times a day for three days then 10mg three times a day when required for nausea

24. Ondansetron 8mg oral twice a day for 3 days starting on the evening of day one or treatment

Administration Instructions

Start on the evening of day 1 of the treatment cycle

25. Growth Factor as directed

Administration instructions

Growth factor as per local formulary choice. For example;

filgrastim or bioequivalent 30million units once a day for 5 days starting on day 5 of the cycle subcutaneous

lenograstim or bioequivalent 33.6million units once a day for 5 days starting on day 5 of the cycle subcutaneous

Pegfilgrastim or lipegfilgrastim or bioequivalent 6mg on the day after SACT administration

Cycle 5 onwards

26. Serplulimab 4.5mg/kg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Administration Instructions

Administer the infusion solution intravenously using a sterile, non-pyrogenic, low-protein binding 0.2 to 5.0 µm in-line or add-on filter.

The first infusion should be administered over 100ml/hour. If this is well tolerated subsequent infusions can be administered over 30minutes.

Ensure the patient has been given a serplulimab patient alert card.

27. Chlorphenamine 10mg intravenous injection when required for infusion related reactions

28. Hydrocortisone 100mg intravenous injection when required for infusion related reactions

29. Paracetamol 1000mg oral when required for infusion related reactions

Administration Instructions

Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2026	N/A	Alexandre Guedes Pharmacist	Dr Salma Naheed Consultant

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.