**Chemotherapy Protocol**

# LUNG CANCER – SMALL CELL (SCLC)

**Tarlatamab (EAMS)**

## Regimen

- SCLC – Tarlatamab (EAMS)

## Indication

- Tarlatamab is indicated as monotherapy for the treatment of adult patients with advanced Small Cell Lung Cancer (SCLC) with disease progression on or after platinum-based chemotherapy.
- This is currently an unlicensed drug in the UK, being supplied and administer under a manufacturer's Expanded Access Program, on a named-patient basis.

## Toxicity

| Drug | Adverse Effect |
|---|---|
| Tarlatamab | Cytokine Release Syndrome (CRS), Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), Tumour Lysis Syndrome (TLS), hypersensitivity reactions, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, constipation, nausea, anaemia, neutropenia, thrombocytopenia, lymphopenia, hepatotoxicity, decreased sodium and increased uric acid |

The adverse effects listed are not exhaustive. Please refer to the relevant summary of product characteristics for further details.

Risk of tumour lysis syndrome (TLS) may be increased in patients with a high tumour burden and rapidly growing tumour. Please follow the relevant hospital guidelines for the assessment, prophylaxis and management of TLS when required.

Severe CRS and ICANS can occur with Tarlatamab. For assessment and management of CRS and ICANS, please refer to the following hospital guidelines:

- Assessment and management of Cytokine Release Syndrome (CRS) following CAR-T Therapy.
- Diagnosis and management of Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) POST CAR-T Therapy.
- Immune Effector Cells including CAR-T cells policy.

## Pre-Assessment

- Record height and weight & performance status (ECOG).
- Blood tests: FBC, U&Es, $Ca^{2+}$ and LFTs at baseline and prior to each dose of treatment.
- Consent and counselling - ensure patient has received adequate verbal and written information regarding their disease, treatment, and potential side effects. Document in medical notes all information that has been given. Obtain written consent prior to treatment.
- Treatment should be agreed in the relevant MDT.

## Monitoring

- It is advisable to admit patients as an inpatient during the step-up dosing period (Cycle 1, days 1 and 8) due to the risk of cytokine release syndrome (CRS) and Immune-Effector Cell Associated Neurotoxic Syndrome (ICANS).
- Follow monitoring recommendations detailed on “Protocol” section below, during and after each Tarlatamab administration.

## Dose Modifications

No dose reductions for Tarlatamab are recommended. Please see the recommended actions on the tables below

Any treatment changes should be discussed with the relevant consultant before prescribing if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

### *Haematological*

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L).

**Table 1**

| Neutrophils ($x10^9$ /L) | **Actions** |
|---|---|
| Less than 1.0 or Febrile neutropenia | Withhold Tarlatamab until neutrophil count improves to at least 1.0 $x10^9$ /L and fever resolves. Consider administration of granulocyte colony stimulating factor (GCSF)<br>Permanently discontinue if recovery does not occur within 3 weeks. |
| Recurrent grade 4 neutropenia (less than 0.5) | Permanently discontinue Tarlatamab |
| Platelets ($x10^9$ /L) | **Actions** |
| Less than 50 | Withhold Tarlatamab until platelet count improves to at least 50 $x10^9$ /L and no evidence of bleeding.<br>Permanently discontinue if recovery does not occur within 3 weeks. |

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|---|---|
| Recurrent grade 4 thrombocytopenia (less than 25) | Permanently discontinue Tarlatamab |
| Haemoglobin (x g/dL) | **Actions** |
| Less than 8 | Withhold Tarlatamab until haemoglobin level improves to at least 8 g/dL |

*Hepatic Impairment*

**Table 2**

| **Severity** | **Actions** |
|---|---|
| **Grade 1 or 2** ALT/AST (<5 x ULN) or Bilirubin (<3 x ULN) | No action required |
| Grade 3 increased ALT or AST (>5.0 - 20.0 x ULN)<br>**OR**<br>Grade 3 increased Bilirubin (>3.0 - 10.0 x ULN) | Withhold Tarlatamab until toxicity improves to ≤ Grade 1. |
| Grade 4 increased ALT or AST (>20.0 x ULN)<br>**OR**<br>Grade 4 increased Bilirubin (>10.0 x ULN)<br>**OR**<br>AST or ALT > 3 × ULN with total bilirubin > 2 × ULN in the absence of alternative causes | Permanently discontinue Tarlatamab |

*Renal Impairment*

**Table 3**

| **Severity** | **Actions** |
|---|---|
| CrCl >30 mL/min | No action required |
| CrCl < 30 mL/min | No data available. Use only if benefit outweighs risks. |

*Other toxicities*

**Table 4**

| **Infections** | **Actions** |
|---|---|
| All Grades | Withhold Tarlatamab in the step-up phase in patients with active infection until it resolves. |
| Grade 3 | Withhold Tarlatamab until infection improves to Grade |

| | |
|---|---|
| | 1 or better. |
| Grade 4 | Permanently discontinue Tarlatamab |
| **CRS** | **Actions** |
| **Grade 1**<br>Symptoms require symptomatic treatment only.<br>Temperature ≥38°C without hypotension or hypoxia | Withhold Tarlatamab until adverse reaction resolves, then resume at the next scheduled dose.<br>See "*Assessment and Management of Cytokine Release Syndrome (CRS) following CAR-T Therapy*". |
| **Grade 2**<br>Symptoms require and respond to moderate intervention.<br>Temperature ≥38°C with either<br>Hypotension responsive to fluids and not requiring vasopressors.<br>**OR**<br>Oxygen requirement of ≤6 L/min<br>Grade 3 (Duration < 48 hours)<br>Temperature ≥38°C with either<br>Hypotension requiring one vasopressor with or without vasopressin.<br>**OR**<br>Oxygen requirement of > 6 L/min | Withhold Tarlatamab until adverse reaction resolves, then resume at the next scheduled dose.<br>When resuming treatment at the next planned dose, monitor patient from the start of the Tarlatamab infusion for 24 hours in an appropriate healthcare setting.<br>See "*Assessment and Management of Cytokine Release Syndrome (CRS) following CAR-T Therapy*". |
| **Grade 3**<br>Severe symptoms defined as<br>Recurrent or duration of more than 48 hours<br>Temperature ≥38°C with either<br>Hypotension requiring one vasopressor with or without vasopressin.<br>**OR**<br>Oxygen requirement of > 6 L/min | Withhold Tarlatamab until adverse reaction resolves, then resume at the next scheduled dose.<br>For recurrent Grade 3 events, permanently discontinue Tarlatamab.<br>When resuming treatment at the next planned dose, monitor patient from the start of the Tarlatamab infusion for 24 hours in an appropriate healthcare setting.<br>See "*Assessment and Management of Cytokine Release Syndrome (CRS) following CAR-T Therapy*". |
| Grade 4<br>Temperature ≥38°C with either<br>Hypotension requiring multiple vasopressor (excluding vasopressin)<br>**OR** | Permanently discontinue Tarlatamab.<br>See "*Assessment and Management of Cytokine Release Syndrome (CRS) following CAR-T Therapy*". |

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| Oxygen requirement of positive pressure (i.e. CPAP, BiPAP, intubation, and mechanical ventilation) | |
| **ICANS** | **Actions** |
| **Grade 1**<br>ICE score 7-9b with no depressed level of consciousness. | Withhold Tarlatamab until adverse reaction resolves, then resume at the next scheduled dose.<br>See "*Diagnosis and Management of Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) POST CAR-T Therapy*". |
| **Grade 2**<br>ICE score 3-6b and/or mild somnolence awaking to voice. | Withhold Tarlatamab until adverse reaction resolves, then resume at the next scheduled dose.<br>When resuming treatment at the next planned dose, monitor patient from the start of the Tarlatamab infusion for 24 hours in an appropriate healthcare setting.<br>See "*Diagnosis and Management of Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) POST CAR-T Therapy*". |
| **Grade 3**<br>ICE score 0-2<br>**AND/OR**<br>depressed level of consciousness awakening only to tactile stimulus.<br>**AND/OR**<br>Any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention.<br>**AND/OR**<br>Focal or local oedema on neuroimaging. | Withhold Tarlatamab until adverse reaction resolves, then resume at the next scheduled dose.<br>If no improvement to grade ≤ 1 within 7 days or recurrent grade 3 toxicity, permanently discontinue Tarlatamab.<br>Recommended intensive monitoring (ICU care).<br>When resuming treatment at the next planned dose, monitor patient from the start of the Tarlatamab infusion for 24 hours in an appropriate healthcare setting.<br>See "*Diagnosis and Management of Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) POST CAR-T Therapy*". |
| **Grade 4**<br>ICE score 0 (patient is unarousable and unable to perform ICE);<br>**AND/OR**<br>Stupor or coma;<br>**AND/OR**<br>Life-threatening prolonged seizure (>5 minutes) or repetitive clinical or electrical seizures without return to baseline in between;<br>**AND/OR**<br>diffuse cerebral oedema on | Permanent discontinuation.<br>ICU care.<br>Treat convulsive status epilepticus as per local guidelines.<br>See "*Diagnosis and Management of Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) POST CAR-T Therapy*". |

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|---|---|
| neuroimaging, decerebrate or decorticate posturing or papilledema, cranial nerve VI palsy, or Cushing's triad. | |
| Other Adverse Reactions | **Actions** |
| Grade 3 and 4 | Withhold Tarlatamab until recovery to ≤Grade 1 or baseline. Consider permanently discontinuing if adverse reaction does not resolve within 28 days. Consider permanent discontinuation for Grade 4 events. |

*Hypersensitivity reactions*

Hypersensitivity reactions have been reported in patients treated with tarlatamab including rare severe events. Clinical signs and symptoms of hypersensitivity may include but are not limited to rash and bronchospasm. Monitor patients for signs and symptoms of hypersensitivity during treatment with tarlatamab and manage as clinically indicated. Withhold or consider permanent discontinuation of tarlatamab based on severity.

Regimen

**28 day cycle until disease progression or intolerable Toxicity (12 cycles will be set on ARIA)**

**Table 5**

| Dosing schedule | | Dose | Monitoring |
|---|---|---|---|
| Cycle 1[a] | Day 1 | 1mg *step-up dose* | Monitor patients from the start of the infusion for 24 hours in an appropriate healthcare setting.<br><br>Recommend that patients remain within 1-hour of an appropriate healthcare setting for a total of 48 hours from start of the infusion accompanied by a caregiver. |
| | Day 8 | 10mg | |
| | Day 15 | 10mg | Observe patients for 6-8 hours post infusion |
| Cycle 2 | Day 1 and 15 | 10mg | Observe patients for 6-8 hours post infusion[b] |
| Cycles 3 and 4 | Day 1 and 15 | 10mg | Observe patients for 3-4 hours post infusion [b] |
| Cycle 5 and subsequent cycles | Day 1 and 15 | 10mg | Observe patients for 2 hours post infusion [b] |

[a] Administer recommended concomitant medications before and after Cycle 1 Tarlatamab infusions as described on Table 7.
[b] Extended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥2 CRS, ICANS or neurological toxicity during prior treatments. See Table 4 for monitoring recommendations.
**Note: see Table 6 for recommendation on restarting tarlatamab after dose delays.**

## Dose Information

- Tarlatamab is available as 1mg and 10mg of lyophilised powder in single-dose vials for reconstitution and further dilution.
- If a dose of Tarlatamab is delayed, treatment should be resumed based on the recommendations listed on the table below. Administer recommended concomitant medications as indicated below [see Additional therapy] and monitor patients accordingly [see Regimen].

**Table 6**

| Last Dose Administered | Time Since the Last Dose Administered | Action |
|---|---|---|
| 1 mg on Cycle 1 Day 1 | 14 days or less | Administer Tarlatamab 10 mg, then resume with the planned dosage schedule. |
| | Over 14 days | Administer Tarlatamab step-up dose 1 mg. If tolerated, increase to 10 mg 1 week later. Then resume with the planned dosage schedule. |
| 10 mg on Cycle 1 Day 8 | 21 days or less | Administer Tarlatamab 10 mg, then resume with the planned dosage schedule. |
| | Over 21 days | Administer Tarlatamab step-up dose 1 mg. If tolerated, increase to 10 mg 1 week later. Then resume with the planned dosage schedule. |
| 10 mg on Cycle 1 Day 15 and subsequent Cycles every 2 weeks thereafter | 28 days or less | Administer Tarlatamab 10 mg, then resume with the planned dosage schedule. |
| | Over 28 days | Administer Tarlatamab step-up dose 1 mg. If tolerated, increase to 10 mg 1 week later. Then resume with the planned dosage schedule. |

## Administration Information

- Tarlatamab should be reconstituted and diluted in 250ml of 0.9% Sodium Chloride and administered as an intravenous infusion over 1 hour at a constant flow rate using an infusion pump.
- The intravenous (IV) catheter used for concomitant medications administration can be used to administer the tarlatamab infusion.
- To ensure patency, flush the IV catheter over 3-5 mins using 0.9% Sodium Chloride for Injection.

## Additional Therapy

- Dexamethasone 8mg IV (or equivalent) and Sodium Chloride 0.9% must be administered on Cycle 1, as per table below:

**Table 7**

| Additional medication | Cycle 1 day 1 | Cycle 1 day 8 | Cycle 1 day 15 |
|---|---|---|---|
| **Dexamethasone 8mg intravenous injection 1 hour prior to Tarlatamab infusion** | √ | √ | |
| **Sodium chloride 0.9% 1000ml intravenous infusion over 60 minutes, starting immediately after completion of Tarlatamab infusion** | √ | √ | √ |

- Premedication may also be required if:
  - Patients who repeat the step-up dosing after delays.
  - Patients who experienced CRS or other infusion reactions in the previous dose.

- Tocilizumab must be prescribed as *when required* in advance of Tarlatamab infusion, in the event of CRS.Tocilizumab (8 mg/kg, maximum dose 800 mg) intravenously 8-hourly if required. *See Assessment and Management of Cytokine Release Syndrome (CRS) following CAR-T Therapy.*
  - One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of Tarlatamab.
  - Follow local procedures for administration.

- Tumour lysis syndrome (TLS) prophylaxis should be prescribed according to the individual patient TLS risk and at consultant review:
  - In high-risk patients, consider 3 mg rasburicase intravenous once prior to first dose Tarlatamab followed by oral allopurinol 300 mg once daily starting the day after rasburicase.
  - For low to moderate risk patients, start allopurinol 300 mg oral (100 mg if renal impairment)
  - This must be assessed prior to Tarlatamab treatment and at each dose increment.

- In the event of Tarlatamab hypersensitivity reactions:
  - hydrocortisone 100mg intravenous when required for the relief of Tarlatamab infusion related reactions.
  - salbutamol 2.5mg nebule when required for Tarlatamab related bronchospasm.

References

BC Cancer Provincial Health Services Authority. *Tarlatamab (interim monograph).* BC Cancer 2024. Available from: http://www.bccancer.bc.ca/drug-database-site/Drug%20Index/Tarlatamab_interim%20monograph.pdf

U.S. Food and Drug Administration (FDA). *IMDELLTRA™ (tarlatamab-dlle)*. FDA 2024. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761344s000lbl.pdf

## REGIMEN SUMMARY

### Tarlatamab (EAMS)

### Cycle 1

### Day 1

1. Warning – Ensure TLS assessment completed.
   - TLS prophylaxis allopurinol supplied as pick-up internal on day 1.
   - Rasburicase if required will need prescribing on Aria internal prescription.

2. Dexamethasone 8mg intravenous injection
   Admin Instructions: To be administered 60 minutes prior to Tarlatamab.

3. Tarlatamab 1mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
   Admin Instructions: Monitor patients from the start of the infusion for 24 hours. It is recommended that patients remain within 1-hour of an appropriate healthcare setting for a total of 48 hours from the start of the infusion accompanied by a caregiver.

4. Sodium chloride 0.9% 1000ml intravenous infusion over 300 minutes
   Admin instructions: to be administered immediately after completion of Tarlatamab infusion.

5. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

6. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

7. Tocilizumab 8mg/kg (maximum 800mg) intravenous 8-hourly if required in the event of CRS. Maximum 3 doses.
   Administration Instructions
   See Trust Protocol for CRS management post Tarlatamab.
   One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of Tarlatamab.
   Follow local procedures for administration

Take home medicines (Day 1)

8. Allopurinol 300mg oral once a day for 28 days.
   In accordance with patient assessment.

### Day 8

9. Warning – Ensure TLS assessment completed.
   - TLS prophylaxis allopurinol supplied as pick-up internal on day 1.
   - Rasburicase if required will need prescribing on Aria internal prescription.

10. Dexamethasone 8mg intravenous injection
    Admin Instructions: To be administered 60 minutes prior to Tarlatamab.

11. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Monitor patients from the start of the infusion for 24 hours. It is recommended that patients remain within 1-hour of an appropriate healthcare setting for a total of 48 hours from the start of the infusion accompanied by a caregiver.

12. Sodium chloride 0.9% 1000ml intravenous infusion over 300 minutes
    Admin instructions: to be administered immediately after completion of Tarlatamab infusion.

13. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

14. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

15. Tocilizumab 8mg/kg (maximum 800mg) intravenous 8-hourly if required in the event of CRS. Maximum 3 doses.
    Administration Instructions
    See Trust Protocol for CRS management post Tarlatamab.
    One dose of tocilizumab must be available on the ward or pre-specified location prior to infusion of Tarlatamab.
    Follow local procedures for administration.

**Day 15**

16. Warning – Ensure TLS assessment completed.
    - TLS prophylaxis allopurinol supplied as pick-up internal from Day 1.
    - Rasburicase if required will need prescribing on in-patient prescribing system

17. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 6-8 hours post infusion.

18. Sodium chloride 0.9% 1000ml intravenous infusion over 300 minutes
    Admin instructions: to be administered immediately after completion of Tarlatamab infusion.

19. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

20. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

**Cycle 2**

**Day 1**

21. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 6-8 hours post infusion.

22. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

23. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

**Day 15**

24. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 6-8 hours post infusion.

25. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

26. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

### Cycle 3

### Day 1

27. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 3-4 hours post infusion.

28. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

29. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

### Day 15

30. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 3-4 hours post infusion.

31. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

32. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

### Cycle 4

### Day 1

33. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 3-4 hours post infusion.

34. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

35. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

### Day 15

36. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 3-4 hours post infusion.

37. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

38. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

### Cycle 5 onwards

### Day 1

39. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 2 hours post infusion.

40. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

41. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

**Day 15**

42. Tarlatamab 10mg intravenous infusion in 250ml sodium chloride 0.9% over 1 hour
    Admin Instructions: Observe patients for 2 hours post infusion.

43. Hydrocortisone 100mg intravenous once only when required for the relief of Tarlatamab infusion related reactions

44. Salbutamol 2.5mg nebule once only when required for the relief of Tarlatamab related bronchospasm

## DOCUMENT CONTROL

| Version | Date | Amendment | Written By | Approved By |
|---|---|---|---|---|
| 1.0 | 07 February 2025 | | Alexandre Guedes (Pharmacist) | Dr Judith Cave |

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 Hospital 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 that occur as a result of following these guidelines.