Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

OSIMERTINIB-CARBOPLATIN-PEMETREXED

Regimen

- NSCLC – Osimertinib-Carboplatin-Pemetrexed

Indication

- First line therapy for advanced non-small-cell lung cancer (NSCLC) in adults whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
- WHO Performance status 0, 1
- Palliative intent

Toxicity

Drug	Adverse Effect
Carboplatin	Neuropathy, thrombocytopenia
Pemetrexed	Diarrhoea, skin reactions, neuropathy
Osimertinib	Interstitial lung disease (ILD), diarrhoea, stomatitis, rash, dry skin, paronychia, pruritis, thrombocytopenia, leucopenia, neutropenia.

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

Monitoring

Disease

- A baseline chest x-ray should be performed before starting treatment and up to date (ideally within 1 month) cross section imaging should also be performed
- T790M mutation status using a validated test should be performed using either tumour DNA derived from a tissue sample or circulating tumour DNA (ctDNA) obtained from a plasma sample.
- Baseline CT of chest and abdomen. Chest X-ray and CT scan as clinically indicated thereafter.

Regimen

- Baseline cardiac history assessment and ECG for all patients, plus echocardiogram if clinical concerns regarding cardiac issues. Repeat ECG pre cycle 2 then afterwards in case of clinical concern or when patients start on new QTc prolonging medications.

- Toxicity review and blood tests (FBC, LFTs and U&Es) at baseline and then prior to each cycle of treatment thereafter.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function 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. The following is a general guide only.

Haematology

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

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).

Neutrophils ($x10^9$/L)		**Platelets ($x10^9$/L)**	**Dose Modifications**
less than 1.5	and / or	less than 100	Withold treatment **For carboplatin and pemetrexed:** If recovery within 1 week, restart treatment at the initial dose, otherwise continue with 20% dose reduction. If platelets fall below 50x109/L reduce dose by 50%. If myelosuppression recurs despite dose reduction then discontinue treatment. **For Osimertinib:** If recovery to NCI-CTC grade 0-2 occurs within 3 weeks, restart osimertinib at 80mg or lower dose of 40mg, otherwise discontinue osimertinib.

Hepatic Impairment

Drug	Recommendation
Carboplatin	No dose reduction necessary
Pemetrexed	Clinical decision
Osimertinib	**Mild hepatic impairment:** No modification generally required, however, consider stopping treatment if AST/ALT levels are elevated to NCI-CT grade 3 or above, irrespective of the bilirubin **Moderate to severe hepatic impairment:** Discontinue osimertinib treatment

Renal Impairment

Drug	Dose (% of original dose)
Carboplatin	Significant changes in GFR (of more than 10%) may require dose adjustment Do not administer if the CrCl is less than 20ml/min
Pemetrexed	If the creatinine clearance falls below 45ml/min consider dose reduction
Osimertinib	No dose adjustment necessary for mild to moderate renal impairment. Use with caution in severe renal impairment

Pulmonary

Severe, life-threatening or fatal ILD or ILD-like adverse reactions (e.g. pneumonitis) have been observed in patients treated with osimertinib in clinical studies. Most cases improved or resolved with interruption of treatment.

Careful assessment of all patients with an acute onset and/or unexplained worsening of pulmonary symptoms (dyspnoea, cough, fever) should be performed to exclude ILD. Whilst investigations are undertaken, osimertinib should be withheld and permanently discontinued if ILD is diagnosed.

Cardiac

QTc interval	Dose Modifications
Greater than 500msec on at least 2 separate ECGs	Withhold osimertinib until QTc interval is less than 481 msec or recovery to baseline. If baseline QTc is greater than or equal to 481 msec, then restart at a reduced dose (40 mg)
QTc interval prolongation with signs/symptoms of serious arrhythmia	Permanently discontinue osimertinib

Regimen

The starting dose of carboplatin is AUC5 with calculated GFR. The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg. This will be set as 790mg in ARIA to comply with national dose bands. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

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.

21 day cycle until disease progression or intolerance (24 cycles will be set in Aria)

Cycle 1 to 4:

Drug	Dose	Days	Administration
Carboplatin	AUC 5	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Pemetrexed	500mg/m^2	1	Intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
Osimertinib	80mg	1-21	Oral Available as 40mg and 80mg tablets.

Cycle 5 onwards:

Drug	Dose	Days	Administration
Pemetrexed	500mg/m^2	1	Intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
Osimertinib	80mg	1-21	Oral Available as 40mg and 80mg tablets.

Dose Information

- Carboplatin will be dose banded according to the national dose band (10mg/ml)
- The maximum dose will be set at 790mg to comply with national dose bands
- Pemetrexed will be dose banded in accordance with the national dose bands
- Osimertinib is available as 40mg and 80mg film-coated tablets.
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Administration Information

- Carboplatin should be administered 30 minutes after the end of the pemetrexed infusion
- Pemetrexed may be administered in 100ml of either glucose 5% or sodium chloride 0.9% over 10 minutes. The choice of fluid will be dependant on the product stocked by pharmacy. The fluid and volume will not appear in the prescription but can be located in the instructions notepad.
- Osimertinib can be taken either with or without food, at the same time each day.
- If a dose of osimertinib is missed, it should be made up unless the next dose is due within 12 hours.
- Osimertinib should be swallowed whole, with water and not crushed, split or chewed.
- If the patient is unable to swallow the tablet, the tablet may first be dispersed in 50 mL of non-carbonated water. It should be dropped in the water, without crushing, stirred until dispersed and immediately swallowed. An additional half a glass of water should be added to ensure that no residue remains and then immediately swallowed. No other liquids should be added.
- If administration via nasogastric tube is required, the same process as above should be followed but using volumes of 15 mL for the initial dispersion and 15 mL for the residue rinses. The resulting 30 mL of liquid should be administered as per the naso-gastric tube manufacturer's instructions with appropriate water flushes. The dispersion and residues should be administered within 30 minutes of the addition of the tablets to water.

Extravasation

- Carboplatin – irritant
- Pemetrexed - inflammitant

Additional Therapy

- Folic acid 5mg once daily starting 1 – 2 weeks prior to and continuing for three weeks after the last dose of pemetrexed.
- Hydroxocobalamin intramuscular injection 1mg every three months starting on cycle 1.
- Antiemetics:
    - 15-30 minutes prior to chemotherapy (cycles 1-4):
        - ondansetron 8mg oral or intravenous
    - 15-30 minutes prior to chemotherapy (cycles 5-24)
        - metoclopramide 10mg oral or intravenous

  Ensure the patient has taken the oral dexamethasone starting the day before pemetrexed. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg intravenous 15-30 minutes before chemotherapy.

As take-home medication:

- dexamethasone 4mg twice a day oral for 3 days starting the day before chemotherapy is due.
- metoclopramide 10mg three times a day when required
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed
- Prophylactic antibiotics can be considered if required

Additional Information

Consideration should be given to draining pleural or peritoneal effusions prior to pemetrexed administration

References

1. National Institute of Clinical Excellence (2025). Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer [TA1060]. London: National Institute for Health and Care Excellence.
2. Astra Zeneca UK Limited (2025). Tagrisso 40mg and 80mg film-coated tablets Summary of Product Characteristics. Online at http://www.medicines.org.uk/emc/medicine/31496, accessed January 2026.
3. Hospira UK Ltd. Carboplatin 10 mg/ml Intravenous Infusion Summary of Product Characteristics. Electronic Medicines Compendium [Internet]. 2024. Online at: https://www.medicines.org.uk/emc/product/3787/smpc, assessed January 2026
4. Genus Pharmaceuticals Ltd. Pemetrexed 25 mg/ml concentrate for solution for infusion Summary of Product Characteristics. Electronic Medicines Compendium [Internet]. 2023. Online at https://www.medicines.org.uk/emc/product/12684/smpc, assessed January 2026

REGIMEN SUMMARY

Osimertinib-Carboplatin-Pemetrexed

Cycles 1-4

Day Minus One

1. Dexamethasone 4mg twice a day oral*

Day One

2. Warning – Check dexamethasone dose
   Administration Instructions
   Ensure patient has taken the oral dexamethasone starting the day before pemetrexed. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg intravenous 15-30 minutes before chemotherapy.

3. Ondansetron 8mg oral or intravenous
   Administration Instructions
   Administer 15-30 minutes prior to SACT. Administer ondansetron 8mg intravenous if required

4. Pemetrexed 500mg/m^2 intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes

5. Carboplatin AUC 5 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   Start 30 minutes after the end of the pemetrexed infusion.
   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.

Take Home Medicines

6. Dexamethasone 4mg twice a day oral for 3 days starting the day before the pemetrexed infusion*

7. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   Please supply 28 tablets or an original pack as appropriate

8. Folic acid 5mg once daily oral
   Administration Instructions
   Please supply 28 tablets or an original pack as appropriate

9. Osimertinib 80mg once a day oral for 21 days
   Administration Information
   Take either with or without food, at the same time each day.
   Oral chemotherapy.

Cycle 5 onwards

Day One

10. Warning – Check dexamethasone dose
    Administration Instructions
    Ensure patient has taken the oral dexamethasone starting the day before pemetrexed. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg intravenous 15-30 minutes before chemotherapy.

11. Metoclopramide 10mg oral or intravenous

12. Pemetrexed 500mg/m^2 intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes

Take Home Medicines

13. Dexamethasone 4mg twice a day oral for 3 days starting the day before the pemetrexed infusion*

14. Metoclopramide 10mg three times a day when required oral
    Administration Instructions
    Please supply 28 tablets or an original pack as appropriate

15. Folic acid 5mg once daily oral
    Administration Instructions
    Please supply 28 tablets or an original pack as appropriate

16. Osimertinib 80mg once a day oral for 21 days
    Administration Information
    Take either with or without food, at the same time each day.
    Oral chemotherapy.

Hydroxocobalamin will not be included as part of the Aria regime and must be prescribed separately on the cycle for which it is due.

* In Aria Planner the dexamethasone 4mg twice daily will appear on days 1, 2, 3 of treatment. This is the supply for the next cycle. The patient should have been given the supply for cycle one in the pre-assessment or consent clinic. The administration instructions reflect this.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.0	January 2026	New protocol	Alexandre Guedes	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 Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS 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.