Amivantamab (subcutaneous) and lazertinib for EGFR mutation positive non small cell

Indication

First line treatment of adult patients with advanced or metastatic non-small cell lung cancer with activating epidermal growth factor receptor exon 19 deletion or exon 21 L858R substitution mutation, in accordance with NICE Technology Appraisal guidance.

Regimen details

Amivantamab administered as a subcutaneous injection in combination with oral lazertinib, in accordance with licensed dosing and NHS availability.

Table 1 – Treatment regimen details

DRUG	DOSE	DILUENT	ROUTE	FREQUENCY/DURATION
Amivantamab (subcutaneous)	Less than 80 kg 1600 mg 80 kg or more 2240 mg	Ready to use	Subcutaneous injection	Weekly for the first 4 weeks, then every 2 weeks
Lazertinib	240 mg	Not applicable	Oral	Once daily, continuous

Cycle frequency

Amivantamab is administered weekly for the first 4 weeks, then every 2 weeks from week 5 onwards.
Lazertinib is administered once daily continuously.

Number of cycles

Treatment is continued until disease progression or unacceptable toxicity.

Administration

Amivantamab is administered as a subcutaneous injection into the abdomen by a healthcare professional with access to appropriate medical support.
The required volume should be injected over approximately 5 minutes.
Injection sites should be rotated. Do not inject into areas that are red, bruised, tender, scarred, tattooed, not intact, or within 5 cm of the umbilicus.
If the patient experiences pain during injection, the delivery rate may be slowed. If pain persists, the remainder of the dose may be administered at an alternative injection site on the opposite side of the abdomen.
Patients should be monitored for administration related reactions during and after administration.
Lazertinib is administered orally once daily. When given on the same day, lazertinib should be taken prior to amivantamab.

Pre-medication

Pre-medication is required to reduce the risk of administration related reactions.
Prior to the initial dose (Week 1 Day 1)
- Antihistamine, chlorphenamine 4mg oral 30 to 60 minutes before
- Antipyretic, paracetamol 1000mg oral 30 to 60 minutes before
- Glucocorticoid, dexamethasone 20 mg oral at least 60 minutes before

Subsequent doses
• Antihistamine and antipyretic are required prior to all subsequent doses
• Glucocorticoid is optional for subsequent doses (for example dexamethasone 10mg)
• Glucocorticoid should be re-initiated after prolonged dose interruptions
• In the event of an administration related reaction, glucocorticoid should be given at the next subsequent dose as per product guidance

Emetogenicity – consult anti-emetic policy for full details

Low Risk (Category C)

Additional supportive medication

Prophylactic anticoagulation is recommended for the first four months of treatment unless contraindicated, in line with product guidance.

Prophylactic measures for skin and nail toxicity should be considered as per local policy and product literature:

Weeks 1-12:
Doxycycline 100mg BD
Weeks 13+:
Clindamycin 1% lotion used on the scalp daily

4% chlorhexidine on the fingernails and toenails daily for 12 months
Ceramide-based moisturiser at least daily for 12 months

Extravasation

N/A

Investigations – pre first cycle

Standard pre-SACT tests

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST) and albumin prior to each cycle for the first 8 weeks, then prior to each cycle or as per clinician instruction.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Table 2 – Standard test result limits for each administration to go ahead

Investigation	**Limit**
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 2.5 x ULN if no liver metastases < 5 x ULN if liver metastases
Albumin	≥ 25 g/L

Dose modifications

Dose reductions of amivantamab subcutaneous formulation are not recommended. Dose interruptions or permanent discontinuation should be undertaken according to the nature and severity of toxicity.
Dose modifications for lazertinib should follow the Summary of Product Characteristics.

Treatment should be withheld or discontinued as follows.

- Administration related reactions
  At the first sign of an administration related reaction, interrupt administration and provide appropriate supportive treatment.
  For Grade 1 to 2 reactions, treatment may be resumed once symptoms resolve.

For recurrent Grade 3 or any Grade 4 reactions, permanently discontinue amivantamab.

- Interstitial lung disease or pneumonitis
  If ILD or pneumonitis is suspected, withhold both amivantamab and lazertinib pending investigation.
  If ILD or pneumonitis is confirmed, permanently discontinue both agents.
- Venous thromboembolic events
  For VTE associated with clinical instability, withhold treatment until the patient is clinically stable, then resume at the discretion of the treating clinician.
  For recurrent VTE despite appropriate anticoagulation, permanently discontinue one agent. Treatment may continue with either amivantamab or lazertinib, but not both.
- Skin and nail toxicity
  For Grade 1 toxicity, continue treatment with supportive care.
  For persistent Grade 2 toxicity, consider dose interruption and supportive measures.
  For Grade 3 toxicity, withhold treatment until recovery to Grade 1 or baseline, then resume.
  For Grade 4 toxicity, permanently discontinue treatment.
- Other Grade 3 or 4 toxicities
  Withhold treatment until toxicity resolves to Grade 1 or baseline.
  Resume treatment at the discretion of the treating clinician or discontinue permanently if toxicity recurs or does not resolve.
- Dose modifications should be managed in line with the Rybrevant and Lazcluze Summary of Product Characteristics.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Administration related reactions
Interstitial lung disease or pneumonitis
Venous thromboembolic events including deep vein thrombosis and pulmonary embolism
Hepatotoxicity
Severe skin reactions including toxic epidermal necrolysis
Severe infections
Ocular toxicity including keratitis

- **Frequently occurring side effects**

Rash including acneiform dermatitis
Pruritus
Dry skin
Nail toxicity including paronychia
Hypoalbuminaemia
Oedema
Stomatitis
Diarrhoea
Constipation
Nausea
Fatigue
Decreased appetite
Paraesthesia

- **Other side effects**

Headache
Dizziness
Epistaxis
Hypertension
Cough
Dyspnoea
Musculoskeletal pain

Significant drug interactions – for full details consult product literature/ reference texts

- Live or live attenuated vaccines should be avoided during treatment with amivantamab.

- Lazertinib is metabolised via CYP3A4. Concomitant use with strong CYP3A4 inducers, including rifampicin, carbamazepine, phenytoin, and St John's wort, should be avoided due to reduced exposure.
- Caution is required when lazertinib is co administered with medicinal products that are substrates of CYP3A4 or breast cancer resistance protein, particularly those with a narrow therapeutic index, as exposure may be increased.
- Systemic corticosteroids and other immunosuppressive agents may interfere with the efficacy of treatment when used at baseline and should be avoided where possible. Corticosteroids may be used to manage treatment related toxicities.
- Anticoagulants should be used with caution due to the increased risk of bleeding. Patients receiving prophylactic anticoagulation should be monitored closely.

Additional comments

- Prophylactic anticoagulation is recommended for the first four months of treatment unless contraindicated, due to the increased risk of venous thromboembolism with this regimen.
- Patients should be counselled regarding the risk of skin, nail, and ocular toxicity and advised to report symptoms early. Preventive skin care measures and sun protection are recommended.
- Patients should be advised to report new or worsening respiratory symptoms promptly due to the risk of interstitial lung disease or pneumonitis.
- Adequate contraception should be used during treatment and for at least three months after the last dose.
- This regimen should be prescribed and administered by clinicians experienced in the use of systemic anticancer therapies, with access to appropriate facilities for the management of treatment related toxicities.

References

1. NICE Technology Appraisal. Amivantamab with lazertinib for untreated epidermal growth factor receptor mutation positive advanced non small cell lung cancer. Final draft guidance, December 2025.
2. Rybrevant subcutaneous formulation. Summary of Product Characteristics. Janssen Cilag Ltd, UK.
3. Lazcluze (lazertinib). Summary of Product Characteristics. Janssen Cilag Ltd, UK.
4. Cho BC, Felip E, Hayashi H, et al. MARIPOSA. Phase III study of amivantamab plus lazertinib versus osimertinib in first line EGFR mutated advanced non small cell lung cancer. Journal of Thoracic Oncology.
5. Cho BC, et al. J Thorac Oncol. 2025;20(10):1517–1530. Enhanced Versus Standard Dermatologic Management With Amivantamab-Lazertinib in EGFR-Mutated Advanced NSCLC: The COCOON Global Randomized Controlled Trial