BISPECIFIC ANTIBODY THERAPY	
Indication	For the first line treatment of locally advanced or metastatic non-small cell lung cancer that exhibits epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations. NB the patient should have had no prior treatment with an EGFR inhibitor unless osimertinib has had to be stopped within 6 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression, or osimertinib has been received as adjuvant treatment for resected stages IB to N2 only IIIB NSCLC with either an EGFR exon 19 deletion or exon 21 substitution mutation and the patient did not progress whilst still receiving adjuvant Osimertinib, or within 12 months of the last dose of osimertinib being taken.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days. Continue until disease progression or excessive toxicity or patient choice to discontinue. NB If a patient experiences severe toxicity specifically related to amivantamab, lazertinib can be continued as a single agent. NB treatment should be stopped if there is disease progression in the CNS that cannot be treated with surgery or stereotactic radiotherapy.
Monitoring Parameters	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • **Haematological monitoring:** ○ **FBC, U&Es** (in particular potassium, calcium and magnesium) and **LFTS** at baseline, day 1 and day 15 of cycle 1 and then day 1 of subsequent cycles. If neuts <1.0 or PLTs <75 discuss with consultant. • **Hepatic impairment:** ○ **Amivantamab:** No formal studies of amivantamab in patients with hepatic impairment have been conducted. Based on population pharmacokinetic (PK) analyses, no dose adjustment is necessary for patients with mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN) or (ULN < total bilirubin </= 1.5 x ULN). Caution is required in patients with moderate (1.5×ULN < total bilirubin </= 3×ULN and any AST) or severe hepatic impairment (total bilirubin > 3 times ULN) as amivantamab has not been studied in this patient population. If treatment is started, patients should be monitored for adverse reactions with dose modifications as indicated (see table 3). ○ **Lazertinib:** No dose adjustment is required in mild (total bilirubin </= ULN and AST > ULN or ULN < total bilirubin </= 1.5×ULN and any AST) or moderate impairment (1.5×ULN < total bilirubin </= 3×ULN and any AST). The pharmacokinetics (PK) of lazertinib in patients with severe hepatic impairment (total bilirubin > 3×ULN and any AST) is unknown. Caution is required in patients with severe hepatic impairment. • **Renal impairment:** ○ **Amivantamab:** No formal studies have been conducted. Based on population pharmacokinetic (PK) analyses, no dose adjustment is necessary for patients with mild or moderate impairment. Caution is required in patients with severe renal impairment due to lack of data. If treatment is started, patients should be monitored for adverse reactions. ○ **Lazertinib**: No formal studies have been conducted. Based on population pharmacokinetic (PK) analyses, no dose adjustment is necessary for patients with mild, moderate or severe

impairment. The pharmacokinetics (PK) of lazertinib in patients with end stage renal disease is unknown.

- **Amivantamab Injection related reactions:**
  - Pause or slow delivery rate if the patient experiences pain. In the event pain is not alleviated by pausing or slowing down delivery rate, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.
  - At the first sign of administration-related reactions of any severity, injections should be interrupted, if ongoing, and post-injection medicinal products should be administered as clinically indicated. For grade 1 to 3, upon resolution of symptoms, the injection should be resumed. Additional supportive medicinal products should be administered at next dose as clinically indicated, including dexamethasone 20mg.
  - For Grade 4 or recurrent Grade 3 administration-related reactions, amivantamab should be permanently discontinued.
- **Management of adverse reactions:**
- **Skin / nail reactions:**
  - If Grade 1-2 skin or nail reaction occurs, supportive care should be initiated; if there is no improvement after 2 weeks, dose reduction should be considered for persistent Grade 2 rash (see Table 3).
  - If Grade 3 or poorly tolerated Grade 2 skin or nail reaction occurs, supportive care should be initiated (systemic antibiotics and oral steroids), and interruption of amivantamab and lazertinib should be considered until the adverse reaction improves. See table 3 for guidance.
  - Patients presenting with severe rash that has an atypical appearance or distribution or lack improvement within 2 weeks should be referred promptly to a dermatologist. TEN has been reported with this treatment. If the patient develops Grade 4 skin reactions, permanently discontinue amivantamab and See table 3 for guidance on administration of lazertinib.
  - Patients should be instructed to limit sun exposure during and for 2 months after amivantamab / lazertinib treatment. Patients should be advised to use broad-spectrum sunscreen (SPF >/=30) and to wear protective clothing to include sunglasses/sunhat.
  - Alcohol-free emollient cream is recommended for dry areas of skin.
- **Venous thromboembolic (VTE) events:**
  - VTE events, including deep vein thrombosis (DVT) and pulmonary embolism (PE), were reported in patients receiving amivantamab in combination with lazertinib.
  - VTE events predominantly occurred in the first 4 months of treatment, prophylactic anticoagulants are recommended to be used for the first four months of treatment.
  - Monitor for signs and symptoms of VTE events. Patients with VTE events should be treated with anticoagulation as clinically indicated.
  - For VTE events associated with clinical instability (e.g., respiratory failure or cardiac dysfunction), both drugs should be withheld until the patient is clinically stable. Thereafter, treatment can be resumed at the same dose, at the discretion of the treating physician. In the event of recurrence despite therapeutic level anticoagulation, combination therapy should be permanently discontinued. Monotherapy can continue with either amivantamab or lazertinib at clinician's discretion.
- **Interstitial lung disease (ILD)**
- ILD or ILD-like adverse reactions (e.g., pneumonitis) have been reported in patients treated with amivantamab and lazertinib, including fatal events. Patients should be monitored for symptoms indicative of ILD/pneumonitis (e.g., dyspnoea, cough, fever). Amivantamab and lazertinib should be withheld if ILD or ILD-like adverse reactions (pneumonitis) is suspected. If the patient is confirmed to have ILD or ILD-like adverse reactions (e.g., pneumonitis), permanently discontinue.
- **Keratitis:** Patients presenting with worsening eye symptoms should be referred to an ophthalmologist and should discontinue use of contact lenses until symptoms are evaluated.
- **Dose Modification:**
  - If a patient experiences severe toxicity specifically related to amivantamab, lazertinib can be continued as a single agent.

	○ **Amivantamab:** Dosing should be interrupted for Grade 3 or 4 adverse reactions until the adverse reaction resolves to </= Grade 1 or baseline. If an interruption is 7 days or less, restart at the current dose. If an interruption is longer than 7 days, it is recommended restarting at a reduced dose as presented in Table 1. For specific dose modifications for specific adverse reactions see Table 3. ○ **Lazertinib:** For dose modification see table 2 and for specific dose modifications for specific adverse reactions see Table 3. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Lazertinib:** ○ Co-administration of lazertinib with strong CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St. John's wort) should be avoided. ○ Concomitant use of lazertinib with substrates of CYP3A4 and BRCP (sunitinib) can result in higher exposure to these medications. Close monitoring for adverse reactions should be undertaken when substrates with a narrow therapeutic range (cyclosporine, everolimus, pimozide, quinidine, sirolimus, tacrolimus) are co-administered. ○ **Amivantamab:** no formal drug studies have been performed. ○ Avoid the use of live or live-attenuated vaccines while patients are taking amivantamab. • **Missed dose:** ○ **Amivantamab:** if a dose is missed between Weeks 1 to 4, it should be administered within 24 hours. If a dose is missed from Week 5 onward, it should be administered within 7 days. Otherwise, the missed dose should not be administered and the next dose should be administered per the usual dosing schedule. ○ **Lazertinib:** If a dose is missed, it can be administered within 12 hours. If more than 12 hours have passed since the dose was to be given, the missed dose should not be administered and the next dose should be administered per the usual dosing schedule. • **Driving and machinery:** Dizziness, fatigue and visual impairment have been reported in patients treated with amivantamab, if patients experience symptoms it is recommended that they do not drive or use machines until the effect subsides. • **Pregnancy and contraception:** ○ Women of childbearing potential should use effective contraception during lazertinib treatment and up to 3 weeks after treatment. Male patients with female partners of reproductive potential should be advised to use effective contraception (e.g., condom) and not donate or store semen during treatment and for 3 weeks after the last dose of lazertinib. ○ Women of childbearing potential should use effective contraception during amivantamab treatment and for 3 months after cessation of treatment. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	CDF list accessed online 29.12.2025 V1.380 BlueTeq form accessed online 29.12.2025 SPC Lazcluze® accessed online 30.12.2025 SPC Rybrevant® accessed online 29.12.2025 LUNG NOG 03.02.2026 COCOON trial https://www.jto.org/article/S1556-0864(25)00939-6/fulltext

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1: Recommended amivantamab dose modifications for adverse reactions			
Dose*	**Dose after 1st interruption for adverse reaction**	**Dose after 2nd interruption for adverse reaction**	**Dose after 3rd interruption for adverse reaction**
1600 mg	1050 mg	700 mg	Discontinue
2240 mg	1600 mg	1050 mg	
* Dose at which the adverse reaction occurred			

Table 2: Recommended lazertinib dose modification for adverse reactions	
Dose reduction	**Recommended dosage**
Initial dose	240 mg once daily
1st dose reduction	160 mg once daily
2nd dose reduction	80 mg once daily
3rd dose reduction	Discontinue

Table 3: Recommended lazertinib and amivantamab dose modifications for adverse reactions		
Adverse reaction	**Severity**	**Dose modification**
Interstitial lung disease (ILD)	Any grade	• Withhold lazertinib and amivantamab if ILD/pneumonitis is suspected. • Permanently discontinue lazertinib and amivantamab if ILD/pneumonitis is confirmed.
Venous thromboembolic (VTE) events	Events with clinical instability (e.g., respiratory failure or cardiac dysfunction)	• Withhold lazertinib and amivantamab until the patient is clinically stable. Thereafter, both medicinal products can be resumed at the same dose, at the discretion of the treating physician.
	Recurrent VTE event despite therapeutic level anticoagulation	• Permanently discontinue lazertinib or amivantamab. Treatment can resume with either lazertinib or amivantamab, but not both, at the discretion of the treating physician.
Skin and nail reactions	Grade 1	• Supportive care should be initiated. • Reassess after 2 weeks.
	Grade 2	• Supportive care should be initiated. • If there is no improvement after 2 weeks, reduce amivantamab dose and continue lazertinib. • Reassess every 2 weeks, if no improvement, reduce lazertinib dose until ≤ Grade 1 (Table 2).
	Grade 3	• Supportive care should be initiated. Withhold lazertinib and amivantamab. • Upon recovery to ≤ Grade 2, resume both medicinal products at the same dose or consider dose reduction, preferentially reducing the dose of amivantamab first. • If there is no improvement within 2 weeks, permanently discontinue both lazertinib and amivantamab.
	Grade 4 (including severe bullous, blistering or exfoliating skin conditions)	• Permanently discontinue amivantamab and hold lazertinib. • Withhold lazertinib until ≤ Grade 2 or baseline. • Upon recovery to ≤ Grade 2, resume lazertinib at the same dose or consider dose reduction.
Other adverse reactions	Grade 3-4	• Withhold lazertinib and amivantamab until the adverse reaction resolves to ≤ Grade 1 or baseline. • Resume one or both medicinal products, preferentially resuming lazertinib first at a reduced dose, unless the adverse reaction is strongly suspected to be related to lazertinib. • Consider permanently discontinuing both lazertinib and amivantamab if recovery does not occur within 4 weeks.

Cycle 1 only: 28 days.

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone*	20mg	PO	stat	Given at least 1 hour prior to the amivantamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	Ensure patient has taken lazertinib dose.				
	AMIVANTAMAB	**<80kg 1600mg**** **>/=80kg 2240mg****	Sub cut	5 minutes	Inject into the subcutaneous tissue of the abdomen only. Do not administer at other sites. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 5 cm around the periumbilical area. Injection sites should be rotated for successive injections. If administering with a subcutaneous infusion set, ensure that the full dose is delivered through the infusion set. Sodium chloride 9 mg/mL (0.9%) solution may be utilised to flush remaining medicinal product through the line. Use of a 21G to 23G needle or infusion set is recommended.
	****AMIVANTAMAB DOSE** is to be calculated on baseline weight, **NO** dose adjustment required for changes in weight during treatment.				
8	Dexamethasone*	10mg	PO	stat	Given at least 1 hour prior to the amivantamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	Ensure patient has taken lazertinib dose.				
	AMIVANTAMAB	**<80kg 1600mg**** **>/=80kg 2240mg****	Sub cut	5 minutes	Inject into the subcutaneous tissue of the abdomen only. Do not administer at other sites. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 5 cm around the periumbilical area. Injection sites should be rotated for successive injections. If administering with a subcutaneous infusion set, ensure that the full dose is delivered through the infusion set. Sodium chloride 9 mg/mL (0.9%) solution may be utilised to flush remaining medicinal product through the line. Use of a 21G to 23G needle or infusion set is recommended.
	****AMIVANTAMAB DOSE** is to be calculated on baseline weight, **NO** dose adjustment required for changes in weight during treatment.				

15	Dexamethasone*	10mg	PO	stat	Given at least 1 hour prior to the amivantamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	Ensure patient has taken lazertinib dose.				
	AMIVANTAMAB	**<80kg 1600mg**** **>/=80kg 2240mg****	Sub cut	5 minutes	Inject into the subcutaneous tissue of the abdomen only. Do not administer at other sites. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 5 cm around the periumbilical area. Injection sites should be rotated for successive injections. If administering with a subcutaneous infusion set, ensure that the full dose is delivered through the infusion set. Sodium chloride 9 mg/mL (0.9%) solution may be utilised to flush remaining medicinal product through the line. Use of a 21G to 23G needle or infusion set is recommended.
	****AMIVANTAMAB DOSE** is to be calculated on baseline weight, **NO** dose adjustment required for changes in weight during treatment.				
22	Dexamethasone*	10mg	PO	stat	Given at least 1 hour prior to the amivantamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	Ensure patient has taken lazertinib dose.				
	AMIVANTAMAB	**<80kg 1600mg**** **>/=80kg 2240mg****	Sub cut	5 minutes	Inject into the subcutaneous tissue of the abdomen only. Do not administer at other sites. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 5 cm around the periumbilical area. Injection sites should be rotated for successive injections. If administering with a subcutaneous infusion set, ensure that the full dose is delivered through the infusion set. Sodium chloride 9 mg/mL (0.9%) solution may be utilised to flush remaining medicinal product through the line. Use of a 21G to 23G needle or infusion set is recommended.
	****AMIVANTAMAB DOSE** is to be calculated on baseline weight, **NO** dose adjustment required for changes in weight during treatment.				

*dexamethasone pre-med can be omitted or reduced to 10mg from Cycle 1 day 8 (second dose of amivantamab), if treatment has been withheld for a prolonged period dexamethasone 20mg pre-med should be given.

TTOS cycle 1

TTO	Drug	Dose	Route	Directions
Day 1	**LAZERTINIB**	**240mg**	PO	OD continuously Swallow whole with or without food. Do not crush, split, or chew the tablets. When taking on the same day as amivantamab administration take any time prior to the amivantamab dose. Available as 240mg and 80mg tablets.
	Doxycycline	100mg	PO	BD For the first 12 weeks of treatment. **Cycle 1 to 3 only.**
	Apixaban	2.5mg	PO	BD For the first 16 weeks of treatment. **Cycle 1 to 4 only.**
	Cetraben Cream		topical	Apply daily and as required to the face and body avoiding the scalp. Continue for 12 months after starting treatment.
	Chlorhexidine gluconate solution	4%	topical	OD Use as wash for hands and feet once a day, to include fingernails and toenails. Continue for 12 months after starting treatment.
	Hydrocortisone cream	1%	topical	Apply as directed to the affected area daily if rash occurs. Dispense on cycle 1 then only if required.
	Metoclopramide	10mg	PO	Take 10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously
	Loperamide	2mg-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on **Cycle 1** then only if required.

Cycle 2 onwards: repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone*	10mg	PO	stat	Given at least 1 hour prior to the amivantamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	Ensure patient has taken lazertinib dose.				
	AMIVANTAMAB	**<80kg 1600mg**** **>/=80kg 2240mg****	Sub cut	5 minutes	Inject into the subcutaneous tissue of the abdomen only. Do not administer at other sites. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 5 cm around the periumbilical area. Injection sites should be rotated for successive injections. If administering with a subcutaneous infusion set, ensure that the full dose is delivered through the infusion set. Sodium chloride 9 mg/mL (0.9%) solution may be utilised to flush remaining medicinal product through the line. Use of a 21G to 23G needle or infusion set is recommended.
	****AMIVANTAMAB DOSE** is to be calculated on baseline weight, **NO** dose adjustment required for changes in weight during treatment.				
15	Dexamethasone*	10mg	PO	stat	Given at least 1 hour prior to the amivantamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	Ensure patient has taken lazertinib dose.				
	AMIVANTAMAB	**<80kg 1600mg**** **>/=80kg 2240mg****	Sub cut	5 minutes	Inject into the subcutaneous tissue of the abdomen only. Do not administer at other sites. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 5 cm around the periumbilical area. Injection sites should be rotated for successive injections. If administering with a subcutaneous infusion set, ensure that the full dose is delivered through the infusion set. Sodium chloride 9 mg/mL (0.9%) solution may be utilised to flush remaining medicinal product through the line. Use of a 21G to 23G needle or infusion set is recommended.
	****AMIVANTAMAB DOSE** is to be calculated on baseline weight, **NO** dose adjustment required for changes in weight during treatment.				

*dexamethasone pre-med can be omitted or reduced to 10mg from Cycle 1 day 8 (second dose of amivantamab), if treatment has been withheld for a prolonged period dexamethasone 20mg pre-med should be given.

TTO cycle 2 onwards

TTO	Drug	Dose	Route	Directions
Day 1	**LAZERTINIB**	240mg	PO	OD continuously Swallow whole with or without food. Do not crush, split, or chew the tablets. When taking on the same day as amivantamab administration take any time prior to the amivantamab dose. Available as 240mg and 80mg tablets.
	Doxycycline	100mg	PO	BD For the first 12 weeks of treatment. **Cycle 1 to 3 only.**
	Apixaban	2.5mg	PO	BD For the first 16 weeks of treatment. **Cycle 1 to 4 only.**
	Clindamycin scalp application	1%	topical	Apply OD **at bedtime** for 9 months. Commence after 12-week oral anti-biotic treatment completed. Dispense from **Cycle 4.**
	Cetraben Cream		topical	Apply daily and as required to the face and body avoiding the scalp. Continue for 12 months after starting treatment.
	Chlorhexidine gluconate solution	4%	topical	OD Use as wash for hands and feet once a day, to include fingernails and toenails. Continue for 12 months after starting treatment.
	Hydrocortisone cream	1%	topical	Apply as directed to the affected area daily if rash occurs. Dispense on cycle 1 then only if required.
	Metoclopramide	10mg	PO	Take 10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously
	Loperamide	2mg-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on **cycle 1** then only if required.