AMIVANTAMAB (Rybrevant) LAZERTINIB (Lazcluze)

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (AMI1)

1. Amivantamab with lazertinib for the first line treatment (no previous cytotoxic chemotherapy or immunotherapy or EGFR inhibitor) of locally advanced or metastatic histologically or cytologically documented non-small cell lung cancer in adults whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations. PS 0 or 1. (TA1122)

REGIMEN

Cycle 1 (administer lazertinib first)

Days 1, 8, 15 and 22	Premedication:
	Chlorphenamine 4mg tablet po (30-60 minutes prior to injection)
	Paracetamol 1000mg tablet po (30-60 minutes prior to injection)
Day 1	Dexamethasone 20mg tablet po (at least 60 minutes prior to injection)
Days 8, 15 and 22	Dexamethasone 10*mg tablet po (optional) (60-90 minutes prior to injection)
Days 1 to 28	LAZERTINIB 240mg orally daily continuously
Days 1, 8, 15 and 22	AMIVANTAMAB <80kg 1600mg, ≥80kg 2240mg subcutaneously over 5 minutes

Cycle 2 onwards (administer lazertinib first)

Days 1 and 15	Premedication:
	Chlorphenamine 4mg tablet po (30-60 minutes prior to injection)
	Paracetamol 1000mg tablet po (30-60 minutes prior to injection)
	Dexamethasone 10*mg tablet po (optional) (60-90 minutes prior to injection)
Days 1 to 28	LAZERTINIB 240mg orally daily continuously
Days 1 and 15	AMIVANTAMAB <80kg 1600mg, ≥80kg 2240mg subcutaneously over 5 minutes

*20mg must be given at the next subsequent dose in the event of an administration related reaction

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression.
If a patient experiences severe toxicity specifically related to amivantamab, lazertinib can be continued as a single agent.

ADMINISTRATION

Subcutaneously over 5 minutes into the abdomen but not within 5cm around the periumbilical area.

ANTI-EMETICS

Low emetic risk

CONCURRENT MEDICATION REQUIRED

Amivantamab	Ensure premedication administered. Chlorphenamine, paracetamol and dexamethasone 20mg before day 1 cycle 1and should also be continued after an administration-related reaction, or re-initiated after prolonged dose interruptions, dexamethasone 10mg for subsequent doses optional. Thromboprophylaxis for the first 4 months of treatment eg DOAC or LMWH (vitamin K analogues are not recommended). Sun exposure should be limited. Alcohol free eg ceramide based emollient cream is recommended for dry areas of skin. Doxycycline 100mg bd cycles 1-3 Clindamycin 1% lotion on scalp once daily cycles 4-13, Chlorhexidine 4% wash od to fingernails and toenails
Lazertinib	Thromboprophylaxis for the first 4 months of treatment eg DOAC or LMWH (vitamin K analogues are not recommended). Sun exposure should be limited. Alcohol free eg ceramide based emollient cream is recommended for dry areas of skin. Doxycycline 100mg bd cycles 1-3 Clindamycin 1% lotion on scalp once daily cycles 4-13, Chlorhexidine 4% wash od to fingernails and toenails

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Creatinine every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Amivantamab	Administration related reactions Eye disorders including keratitis – refer to an ophthalmologist (stop wearing contact lenses) (see dose modifications) Hepatotoxicity Interstitial lung disease Skin and nail reactions Stomatitis Venous thromboembolic events
Lazertinib	Diarrhoea Eye disorders including keratitis – refer to an ophthalmologist (stop wearing contact lenses) Interstitial lung disease Skin and nail reactions Stomatitis Venous thromboembolic events

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Amivantamab	Atezolizumab, avelumab, cemiplimab, cosibelimab, deucravacitinib, dostarlimab, durvalumab, efgartigimod alfa, ipilimumab, nipocalimab, nivolumab, pembrolizumab, penpulimab, retifanlimab, rozanolizizumab, tislelizumab, toripalimab, tremelimumab
Lazertinib	Apalutamide, carbamazepine, encorafenib, enzalutamide, fosphenytoin, ivosidenib, lumacaftor, mitotane, phenobarbital, phenytoin, primidone, rifampicin, st john's wort

DOSE MODIFICATIONS
Non-haematological
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.

Grade 3 or 4 adverse reactions	Amivantamab dose	Amivantamab dose
Dose at which adverse reaction occurred	1600mg	2240mg
1st dose interruption for adverse reaction	1050mg	1600mg
2nd dose interruption for adverse reaction	700mg	1050mg
3rd dose interruption for adverse reaction	discontinue	discontinue

Lazertinib

Level	Lazertinib dose
Initial dose	240mg
1st dose reduction	160mg
2nd dose reduction	80mg
3rd dose reduction	discontinue

Lazertinib

Interstitial lung disease

Any grade	• Withhold lazertinib and amivantamab if ILD/pneumonitis is suspected. • Permanently discontinue lazertinib and amivantamab if ILD/pneumonitis is confirmed.

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.

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
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.

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.

Hepatic impairment

Amivantamab

No formal studies of amivantamab in patients with hepatic impairment have been conducted. Based on population pharmacokinetics analyses, no dose adjustment is necessary for patients with mild hepatic impairment.

Caution is required in patients with moderate or severe hepatic impairment 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 above.

Lazertinib

No dose adjustment is required for patients with mild or moderate hepatic impairment.

The pharmacokinetics of lazertinib in patients with severe hepatic impairment is unknown. Caution is required in patients with severe hepatic impairment.

Renal impairment

Amivantamab

No formal studies of amivantamab in patients with renal impairment have been conducted. Based on population pharmacokinetic analyses, no dose adjustment is necessary for patients with mild or moderate renal impairment.

Caution is required in patients with severe renal impairment 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 above.

Lazertinib

No dose adjustment is required for patients with mild, moderate or severe renal impairment.

The pharmacokinetics of lazertinib in patients with end stage renal disease is unknown.

REFERENCES

1. SPC
2. Cocoon DM