AMIVANTAMAB SC (Rybrevant) PEMETREXED CARBOPLATIN

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/) (AMI2)

1. Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive locally advanced or metastatic, non squamous, non-small-cell lung cancer. PS 0 or 1.

REGIMEN

Cycle 1 (pemetrexed then carboplatin then amivantamab)

Day 1 Pre-medication: Dexamethasone 4mg bd oral for 3 days (starting the day before pemetrexed)

PEMETREXED 500mg/m^2 in #ml IV infusion over 10 minutes

CARBOPLATIN AUC 5 in #ml glucose 5% IV infusion over 30 minutes
Dose calculated by EDTA GFR or calculated CrCl + 25 x AUC.
(Maximum dose when using CrCl 125+25 x AUC)

Premedication:
Chlorphenamine 4mg tablet po (30-60 minutes prior to injection)
Paracetamol 1000mg tablet po (30-60 minutes prior to injection)
Dexamethasone 20mg tablet po (at least 60 minutes prior to injection)

AMIVANTAMAB <80kg** 1600mg, ≥80kg** 2240mg subcutaneously over 5 minutes

Days 8 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)

AMIVANTAMAB <80kg** 2400mg, ≥80kg** 3360mg subcutaneously over 5 minutes

Cycles 2 to 4 (pemetrexed then carboplatin then amivantamab)

Day 1 Pre-medication: Dexamethasone 4mg bd oral for 3 days (starting the day before pemetrexed)

PEMETREXED 500mg/m^2 in #ml IV infusion over 10 minutes

CARBOPLATIN AUC 5 in #ml glucose 5% IV infusion over 30 minutes
Dose calculated by EDTA GFR or calculated CrCl + 25 x AUC.
(Maximum dose when using CrCl 125+25 x AUC)

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)

AMIVANTAMAB <80kg** 2400mg, ≥80kg** 3360mg subcutaneously over 5 minutes

Cycle 5 onwards (pemetrexed then amivantamab)

Day 1 Pre-medication: Dexamethasone 4mg bd oral for 3 days (starting the day before pemetrexed)

PEMETREXED 500mg/m^2 in #ml IV infusion over 10 minutes

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)

AMIVANTAMAB <80kg** 2400mg, ≥80kg** 3360mg subcutaneously over 5 minutes

*20mg must be given at the next subsequent dose in the event of an administration related reaction
** baseline weight
# diluent volume for dose prescribed as per national standardised product specification or licensed dose

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days until disease progression.
If patient experiences severe toxicity specifically related to pemetrexed, amivantamab can be continued as a single agent.

ADMINISTRATION

Subcutaneously over 5 minutes into the abdomen but not within 5cm around the periumbilical area.
First 4 amivantamab missed doses need to be given within 24 hours and 5th dose onwards within 7 days of due dose otherwise to be omitted.

ANTI-EMETICS

Moderate risk day 1 cycles 1 to 4
Low risk day 1 cycle 5 onwards

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. Sun exposure should be limited. Alcohol free eg ceramide based emollient cream is recommended for dry areas of skin. Doxycycline 100mg bd cycles 1-4 Clindamycin 1% lotion on scalp once daily cycles 5-18 Chlorhexidine 4% wash od to fingernails and toenails
Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine 10mg IV bolus Carboplatin should be given at a slower rate e.g. 2-4 hours.
Pemetrexed	Ensure premedication taken: Dexamethasone 4mg bd for 3 days (starting the day before pemetrexed) Folic acid 400mcg/day orally starting 1 to 3 weeks before chemotherapy continuing until 21 days after the last dose of pemetrexed. Hydroxycobalamin 1000mcg IM every 9 weeks starting 1 to 3 weeks before chemotherapy (give with every 3rd cycle of chemotherapy).

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin - irritant
Pemetrexed - inflammatory

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E including Mg^{++} and LFTs every dose
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion. Patients with hydronephrosis or serum creatinine ≥100micromol/L need a serum creatinine checked every cycle.
HB1AC baseline, random glucose
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
Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Pemetrexed	Skin reactions Pneumonitis

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
Pemetrexed	Aminogycosides – increased risk of nephrotoxicity and ototoxicity NSAIDs Avoid all for at least 5 days prior to and 2 days after pemetrexed dose.

DOSE MODIFICATIONS

Haematological

Pemetrexed
Delay treatment until resolution then treat with appropriate dose modification.
Nadir neutrophils <0.5 and nadir platelets >50 — 75% of previous dose
Nadir platelets ≤50 regardless of nadir neutrophils — 50% of previous dose
Treatment with pemetrexed should be discontinued if a patient experiences any haematologic or non-haematologic grade 3 or 4 toxicity after 2 dose reductions

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	Amivantamab dose	Amivantamab dose
Dose at which adverse reaction occurred	1600mg	2240mg	2400mg	3360mg
1st dose interruption for adverse reaction	1050mg	1600mg	1600mg	2240mg
2nd dose interruption for adverse reaction	700mg	1050mg	1050mg	1600mg
3rd dose interruption for adverse reaction	discontinue	discontinue	discontinue	discontinue

Pemetrexed

Any grade 3 or 4 non-haematological toxicities except mucositis	Give 75% of previous dose
Any diarrhoea requiring hospitalisation (irrespective of grade) or grade 3 or 4 diarrhoea	Give 75% of previous dose
Grade 3 or 4 mucositis	Give 50% of previous dose
Neurotoxicity grade 3 or 4	Discontinue therapy
If a patient experiences any haematological or non-haematological grade 3 or 4 toxicity after 2 dose reductions or immediately if grade 3 or 4 neurotoxicity is observed.	Discontinue therapy

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.

Pemetrexed

Total bilirubin should be ≤1.5xULN.

Alk phos, AST and ALT ≤3xULN. (Alk phos, AST, and ALT ≤5x normal is acceptable if liver has tumour involvement). Clinical decision

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.

Carboplatin

GFR / calculated CrCl ≤20ml/min or ≤30ml/min with pre-existing severe renal impairment	Contraindicated

Pemetrexed

CrCl ≤45ml/min	Not recommended

REFERENCES

1. SPC