CEMIPLIMAB (Libtayo) 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/) (CEM2)

1. Cemiplimab with platinum-based chemotherapy for untreated metastatic or advanced non-small-cell lung cancer not suitable for definitive chemoradiation and would be a candidate for pembrolizumab with platinum-based chemotherapy. Stage IIIB or IIIC or IV NSCLC or disease that has recurred more than 6 months after potentially curative treatment with local management of NSCLC with surgery/chemoradiotherapy/radiotherapy. EGFR, ROS1 and ALK negative and PD-L1 positive in 1% or more of the tumour cells. The mandatory interval between the last date of administration of any prior adjuvant/neoadjuvant/maintenance immunotherapy and the date of first relapse is at least 6 months. Has no symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA1165)

REGIMEN

Cycles 1 to 4 Carboplatin to start 30 minutes after completing pemetrexed)

Day 1 CEMIPLIMAB 350mg in 100ml sodium chloride IV infusion over 30 minutes
Pre-medication: Dexamethasone 4mg bd for 3 days (starting the day before chemotherapy)
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)

Cycles 5 to 35

Day 1 CEMIPLIMAB 350mg in 100ml sodium chloride IV infusion over 30 minutes
Pre-medication: Dexamethasone 4mg bd for 3 days (starting the day before chemotherapy)
PEMETREXED 500mg/m^2 in #ml IV infusion over 10 minutes

diluent volume for dose prescribed as per national standardised product specification or licensed dose

Cemiplimab infusion related reactions initiate symptomatic management and for grade 1 or 2 interrupt or slow rate of infusion, for grade 3 or 4 permanently discontinue

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 4 cycles.
Cemiplimab and pemetrexed every 21 days up to maximum 2 years.

ANTI-EMETICS

Moderate risk day 1 cycles 1 to 4
Low risk day 1 cycles 5 to 35

CONCURRENT MEDICATION REQUIRED

Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine10mg 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 chemotherapy) 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
Cemiplimab – neutral (treat symptomatically, non-vesicant, non-irritant but extravasation has occurred)
Pemetrexed IV - inflammatory

Cemiplimab – Use non pyrogenic, low protein binding 0.2 to 5micron in-line or add-on filter.
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E (including Mg^{++}) and LFTs every cycle
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.
Thyroid function* baseline, then every cycle
Random cortisol baseline, then every cycle
Random glucose every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Cemiplimab	Immune related toxicities - pneumonitis, colitis or hepatitis, severe cutaneous adverse reactions etc
Pemetrexed	Skin reactions Pneumonitis

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

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

Cemiplimab

Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline.

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

Cemiplimab

No dose adjustment is recommended for patients with mild or moderate hepatic impairment.
Cemiplimab has not been studied in patients with severe hepatic impairment.

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

Carboplatin

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

Cemiplimab

No dose adjustment of cemiplimab is recommended for patients with renal impairment.
Cemiplimab has not been studied in patients CrCl <21ml/min.

Pemetrexed

CrCl ≤45ml/min	Not recommended

REFERENCES

1. SPC