PEMETREXED CISPLATIN

INDICATION (ICD10) C34

1. Palliative treatment of non-resectable malignant mesothelioma in patient with an ECOG performance status of 0-1. (TA135)
2. First-line treatment of patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) only if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma. PS 0, 1 or 2 (TA181)

REGIMEN

Cisplatin to start 30 minutes after completing pemetrexed

Day 1 Pre-medication: Dexamethasone 4mg bd for 3 days (starting the day before chemotherapy)
PEMETREXED 500mg/m^2 in #ml IV infusion over 10 minutes
CISPLATIN 75mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours

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

CYCLE FREQUENCY AND NUMBER OF CYCLES

Mesothelioma - every 21 days up to 6 cycles
NSCLC - every 21 days 3 to 6 cycles

ANTI-EMETICS

High risk day 1

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
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

Cisplatin - exfoliant
Pemetrexed - inflammatory

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
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 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

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

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

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent) not recommended (palliative intent)
CrCl <40ml/min	not recommended

Pemetrexed

CrCl ≤45ml/min	Not recommended

REFERENCES

1. Vogelzang, N et al; JCO 2003; 21 (14): 2636–2644
2. Scagliotti, GV et al; JCO 2008; 26 (21): 3543–3551