Cisplatin Pemetrexed

Indication

Malignant mesothelioma
Non-small cell lung cancer of predominantly non-squamous histology

Regimen details

Drug	Fluid	Time
Pemetrexed 500mg/m^2	100ml 0.9% sodium chloride	10 minutes
Potassium chloride 20mmol, magnesium sulphate 10mmol	1 litre 0.9% sodium chloride	2 hours
Cisplatin 75mg/m^2	1 litre 0.9% sodium chloride	2 hours
Potassium chloride 20mmol, magnesium sulphate 10mmol	1 litre 0.9% sodium chloride	2 hours

Cycle frequency

Every 21 days

Number of cycles

4-6 cycles

Administration

Pemetrexed should be administered first

Pre-medication

Folic acid 400µg OD orally beginning 1-2 weeks prior to the first dose of pemetrexed continuing 3 weeks after the last dose of pemetrexed.
Vitamin B12 1000µg IM injection 1-2 weeks prior to the first dose of pemetrexed repeated every 9 weeks until 3 weeks after the last dose of pemetrexed.
Dexamethasone 4mg BD should be taken the day before, the day of and the day after treatment.

Emetogenicity

Highly emetogenic

Additional supportive medication

See above

Extravasation

Cisplatin is an exfoliant (Group 4)
Pemetrexed is an inflammitant (Group 2)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Calcium	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), calcium

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 50 mL/min (60 ml/min prior to cycle 1)
Bilirubin	≤ 1.5 x ULN
AST	<3 x ULN or < 5 x ULN in presence of liver metastases
Alkaline phosphatase	<3 x ULN or < 5 x ULN in presence of liver metastases

Dose modifications

Dose modifications

For non-haematological toxicity delay treatment until resolved to ≤ grade 1

Haematological toxicity

If neutrophils < 1.5 x 10^9/L and platelets < 100 x 10^9/L delay for 1 week. If resolved then continue with 100% dose. If 2 or more delays then reduce doses of cisplatin and pemetrexed to 75%.

Renal impairment

CrCl (ml/min)	Cisplatin dose
≥ 60	100%
50-59	75%
40-49	50% (consider switching to carboplatin AUC 5)
< 40	Contraindicated

Pemetrexed should NOT be administered if CrCl <45 ml/min

Hepatic impairment

Pemetrexed: No information available for patients with bilirubin > 1.5 x ULN and/or AST/ALT > 3 x ULN (5 x ULN if liver metastases present) – consultant decision
Cisplatin: No dose modification required

Mucositis

Grade 3-4: reduce pemetrexed to 50% dose and continue with 100% dose cisplatin.

Neurotoxicity

Grade 2: reduce cisplatin to 50% dose and continue with 100% dose pemetrexed.
Grade 3-4: discontinue cisplatin Any other grade 3-4 toxicity: reduce cisplatin and pemetrexed to 75% of previous dose

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Ototoxicity
Nephrotoxicity
Peripheral neuropathy

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Diarrhoea
Oedema
Haematuria

- **Other side effects**

Alopecia
Rash
Fatigue

Significant drug interactions

– for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity when given within 2 weeks of cisplatin.

Diuretics: increased risk of nephrotoxicity and ototoxicity

Nephrotoxic drugs: increased nephrotoxicity; not recommended

Ototoxic drugs: increased risk of ototoxicity

Phenytoin: cisplatin reduces absorption and efficacy of phenytoin, monitor levels and adjust dose as necessary.

Anti-gout agents: cisplatin may increase plasma concentration of uric acid therefore dose adjustments may be required to control hyperuricaemia and gout.

Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided from 5 days before each dose of pemetrexed until 2 days after each dose

Additional comments

References

SWCN chemotherapy protocols - Systemic Anti Cancer Therapy Protocols | (swscn.org.uk)

This protocol has been reviewed by the Lancashire & South Cumbria Lung Oncology Consultants' Group and responsibility for the template lies with the Head of Service

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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