

Pemetrexed single agent

Indication

Maintenance treatment of locally advanced or metastatic non small cell lung cancer (NSCLC), not predominately squamous cell type, who have not progressed immediately after platinum based chemotherapy with gemcitabine, paclitaxel or docetaxel.

(NICE TA190)

Maintenance treatment of locally advanced or metastatic non-squamous non small cell lung cancer (NSCLC), who have not progressed immediately after 4 cycles of pemetrexed and cisplatin induction therapy.

(NICE TA402)

ICD-10 codes

Codes pre-fixed with C34.

Regimen details

Day	Drug	Dose	Route
1	Pemetrexed	500 mg/m ²	IV infusion

Cycle frequency

21 days

Number of cycles

Maintenance therapy until disease progression.

Administration

Pemetrexed is administered in 100mL sodium chloride 0.9% over 10 minutes.

Pre-medication

Vitamin B12 (hydroxycobalamin) 1mg IM in the week preceding the first cycle and then approximately every 9 weeks (i.e. every 3 cycles) until pemetrexed treatment is completed. Pemetrexed should be administered no earlier than 48 hours after vitamin B12 injection for the first dose. Subsequent vitamin B12 injections may be administered on the same day as pemetrexed.

Folic acid 400 microgram PO OD should be started at least 1 week before first cycle (with a minimum of 5 doses taken in the 7 days preceding the first dose) and continued until 3 weeks after last pemetrexed dose.

Dexamethasone 4mg PO BD for 3 days should be started 24 hours before treatment.

Antiemetics as per local guidelines.

Emetogenicity

This regimen has mild emetic potential.

Additional supportive medication

H₂ antagonist or proton pump inhibitor if required.

Mouthwashes as per local policy.

Extravasation

Pemetrexed is an inflammatant (Group 2)

Investigations – pre first cycle

Investigation	Validity period (or as per local practice)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	Validity period (or as per local practice)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

Standard limits for administration to go ahead

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

Investigation	Limit
Neutrophils	$\geq 1.5 \times 10^9/L$
Platelets	$\geq 100 \times 10^9/L$
Creatinine Clearance (CrCl)	> 45 mL/min
Bilirubin	<1.5 x ULN
ALT/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

For non-haematological toxicity delay treatment until resolved to \leq grade 1.

- Haematological toxicity**

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

Where possible subsequent cycles should be modified according to nadir FBC:

Nadir neutrophils < $0.5 \times 10^9/L$ and platelets $\geq 50 \times 10^9/L$ – reduce pemetrexed to 75% of previous dose.

Nadir platelets < $50 \times 10^9/L$ (regardless of neutrophils) – reduce pemetrexed to 50% of previous dose.

- Renal impairment**

CrCl (mL/min)	Pemetrexed dose
≥ 45	100%
< 45	Contraindicated

Pemetrexed should NOT be administered if CrCl <45 mL/min. If this is based on a calculated CrCl patients should have an EDTA creatinine clearance measured.

- Hepatic impairment**

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.

- **Other toxicities**

Mucositis

Grade 3-4: reduce pemetrexed to 50% of previous dose.

Other toxicity

Any other grade 3-4 toxicity: reduce pemetrexed to 75% of previous dose.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression

Infertility

Nephrotoxicity

Peripheral neuropathy

- **Frequently occurring side effects**

Myelosuppression

Mucositis, stomatitis

Diarrhoea

- **Other side effects**

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.

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

- National Institute of Health and Clinical Excellence Guideline TA190. Accessed 20 May 2015 via www.nice.org.uk
- National Institute of Health and Clinical Excellence Guideline TA402. Accessed 21 Dec. 2016 via www.nice.org.uk
- Summary of Product Characteristics Pemetrexed (Lilly) accessed 21 Dec 2016 via www.medicines.org.uk
- Hanna et al; JCO 2004; 22 (9): 1589 – 1597
- Paz-Ares, L et al; Lancet Oncology 2012; 13 (3): 247 - 255

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