

Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

CISPLATIN-PEMBROLIZUMAB-PEMETREXED

Regimen

- NSCLC – Cisplatin-Pembrolizumab-Pemetrexed

Indication

- Pembrolizumab in combination with pemetrexed-based combination chemotherapy for treating untreated PD- L1-positive or negative locally advanced or metastatic non-squamous non-small-cell lung cancer where all the following criteria are met:
 - the patient has a histologically or cytologically-confirmed diagnosis of stage IIIB or IV non-squamous non-small cell lung cancer.
 - EGFR and ALK mutation negative disease
 - PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score (TPS) has been attempted prior to treatment starting
 - the patient has not received previous systemic therapy for advanced / metastatic disease. Completion of treatment with chemotherapy and/or radiotherapy as part of neoadjuvant / adjuvant therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of recurrent locally advanced or metastatic disease
 - the patient will be treated with a maximum of 4 cycles of pembrolizumab plus pemetrexed-based combination chemotherapy with either cisplatin or carboplatin
 - on completion of 4 cycles of pembrolizumab plus pemetrexed-based chemotherapy in combination with cisplatin or carboplatin and in the absence of disease progression, treatment with pembrolizumab in combination with 'maintenance' pemetrexed will continue for a total treatment duration of 2 years (or a maximum of 35 3-weekly cycles) or until disease progression or unacceptable toxicity or withdrawal of patient consent, whichever occurs first.
 - the patient has no symptomatically active brain metastases or leptomeningeal metastases.
 - the patient has not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.
 - a formal medical review as to whether treatment with pembrolizumab in combination with pemetrexed plus cisplatin/carboplatin should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment
 - treatment breaks of up to 12 weeks beyond the expected 3-weekly cycle length are allowed but solely to allow any immune toxicities to settle.
 - the patient has a performance status (PS) of 0 or 1 and is potentially fit for pemetrexed- and platinum-based chemotherapy in combination with pembrolizumab.

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Pembrolizumab	Pneumonitis, nephritis, colitis, thyroid disorders, hypophysitis, infusion related reactions, hepatitis
Pemetrexed	Diarrhoea, skin reactions, neuropathy

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Disease

- A baseline chest x-ray should be performed before starting treatment and up to date (ideally within 1 month) cross section imaging should also be performed

Regimen

- FBC, LFTs and U&Es before each cycle
- EGFR and ALK mutation status prior to starting treatment (cycle one)
- PD-L1 status prior to starting treatment (cycle one)
- Thyroid function tests prior to starting treatment and then before each administration (cycle) or when clinically indicated.
- A chest x-ray should be performed before each cycle
- Consider formal audiology test if relevant

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions with chemotherapy due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Pembrolizumab belongs to the immunotherapy class of cancer treatments. Autoimmune toxicities are most frequently noted and can be life threatening. If autoimmune toxicities occur delaying treatment should be considered while investigations or treatments are organised. Some, but not all, toxicities mandate cessation of treatment. Pembrolizumab dose reductions are not permitted. Pembrolizumab treatment may be interrupted or discontinued due to toxicity.

Please seek guidance from relevant site specific specialist teams or oncologists / haematologists with experience of prescribing these agents. Clinicians should be aware that the current funding approval for pembrolizumab precludes further treatment after an interruption of 12 weeks or longer; this situation may change.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Doses should be adjusted according to the table below;

Dose Level			
	0	-1	-2
Cisplatin	75mg/m ²	56mg/m ²	38mg/m ²
Pemetrexed	500mg/m ²	375mg/m ²	250mg/m ²

Haematology

Prior to prescribing cycle one the following treatment criteria must be met;

Criteria	Eligible Level
Neutrophil	Greater than or equal to 1.5x10 ⁹ /L (unless due to bone marrow impairment)
Platelets	Greater than or equal to 100x10 ⁹ /L (unless due to bone marrow impairment)

Consider blood transfusion or erythropoietin if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/L).

There is little need to adjust the dose of pembrolizumab for haematological toxicity. The following recommendations apply to carboplatin and pemetrexed only.

Dose modifications must be based on the maximum toxicity experienced during a cycle. Toxicity needs to resolve to NCI-CTC grade 1 or below or baseline prior to resuming the next cycle of treatment. For individuals requiring a dose modification, each new cycle may be delayed if the scheduled off-drug periods are not adequate to allow for recovery.

Reduction of one chemotherapy agent and not the other agent is appropriate if the toxicity is clearly related to one of the treatments. If the toxicity is related to the combination of both chemotherapy agents, both drugs should be reduced according to recommended dose modifications.

Dose Modifications for Haematological Toxicity

Platelets (10 ⁹ /L)		Neutrophils (10 ⁹ /L)	Dose Level	
			Cisplatin	Pemetrexed
50 or above	and	0.5 and below	- 1	- 1
49 and below without bleeding	and	Any	- 1	- 1
49 and below with NCI CTC grade 2 bleeding	and	any	- 2	- 2
any	and	0.99 and below with fever	- 1	- 1

Hepatic Impairment

Drug	Recommendation
Cisplatin	No dose reduction necessary
Pembrolizumab	No dose reduction is necessary in those with mild hepatic impairment (see below for hepatic adverse effects)
Pemetrexed	Clinical decision

Renal Impairment

Drug	Dose (% of original dose)	
Cisplatin	more than 60	100
	45-59	75
	less than 45	Consider carboplatin
Pembrolizumab	No dose adjustment is required for mild to moderate renal impairment (see below for renal adverse effects)	
Pemetrexed	If the creatinine clearance falls below 45ml/min consider dose reduction	

Cisplatin and Pemetrexed

	NCI CTC Grade	Cisplatin	Pemetrexed
		Dose Level	
Nausea and Vomiting	3 and above	0	0
Diarrhoea	3 and above	-1	-1
Mucositis	3 and above	0	-2
Neurotoxicity	2	-2	0
	3 and above	Discontinue	-1
Transaminase	3	-1	-1
	4	Discontinue	Discontinue
Other	3 and above	-1	-1

Pembrolizumab

Hepatic Impairment

For a hepatitis associated with an AST / ALT of 3-5xULN and / or a total bilirubin of 1.5-3xULN then withhold treatment and administer corticosteroids. Upon improvement to NCI-CTC grade 1 hepatic injury begin to taper the corticosteroid over a period of one month. The pembrolizumab may be re-started when the liver function remains at NCI-CTC grade 1 following corticosteroid taper.

The pembrolizumab should be permanently discontinued when the hepatic injury does not improve to at least NCI-CTC grade 1 within 12 weeks of the last dose, the

corticosteroid dose cannot be reduced to 10mg or less of prednisolone or equivalent per day within 12 weeks or any NCI-CTC grade 3 or above reaction.

Pembrolizumab should be permanently discontinued in the first instance when hepatitis develops that is associated with an AST / ALT equal to or greater than 5xULN, an increase in AST / ALT of 50% or greater relative to baseline and that lasts at least one week in patients with liver metastasis who begin treatment with moderate (grade 2) elevation of AST / ALT or where the bilirubin is greater than 3xULN.

Renal Impairment

Where a NCI-CTC grade 2 nephritis develops withhold treatment and administer corticosteroids. Upon improvement to NCI-CTC grade 1 or less, initiate corticosteroid taper over at least one month. Pembrolizumab may be resumed when the reaction remains at NCI-CTC grade 1 or below following tapering of the corticosteroid.

The pembrolizumab should be permanently discontinued when the nephritis does not improve to at least NCI-CTC grade 1 within 12 weeks of the last dose, the corticosteroid dose cannot be reduced to 10mg or less of prednisolone or equivalent per day within 12 weeks or any NCI-CTC grade 3 or above reaction.

Pembrolizumab should be permanently discontinued for any NCI-CTC grade 3 or above nephritis.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Pembrolizumab is associated with inflammatory adverse reactions resulting from increased or excessive immune activity, likely to be related to its pharmacology.

Immune-related adverse reactions, which can be severe or life-threatening, may involve the gastrointestinal, liver, skin, nervous, endocrine, or other organ systems. Most occur during treatment, however, onset months after the last dose has been reported. Unless an alternate aetiology has been identified, diarrhoea, increased stool frequency, bloody stool, LFT elevations, rash and endocrinopathy must be considered inflammatory and pembrolizumab-related. Early diagnosis and appropriate management are essential to minimise life threatening complications.

Pembrolizumab should be permanently discontinued for any NCI-CTC grade 3 or 4 pneumonitis, nephritis, infusion related reaction or a NCI-CTC grade 4 adverse reaction.

Endocrine

Pembrolizumab can cause inflammation of the endocrine system organs, specifically hypophysitis, hypopituitarism, adrenal insufficiency, and hypothyroidism. This may present with nonspecific symptoms resembling other causes such as brain metastasis or underlying disease.

Isolated hypothyroidism can be managed with replacement therapy, without treatment interruption or corticosteroids.

If there are any signs of adrenal crisis such as severe dehydration, hypotension, or shock, immediate administration of intravenous corticosteroids with mineralocorticoid activity is recommended, the patient must be evaluated for presence of sepsis or infections. If there are signs of adrenal insufficiency but the patient is not in crisis, further investigations should be considered including laboratory and imaging assessment. Evaluation of laboratory results to assess endocrine function may be performed before corticosteroid therapy is initiated. If pituitary imaging or laboratory tests of endocrine function are abnormal, a short course of high-dose corticosteroid therapy is recommended to treat the gland inflammation. The scheduled dose of pembrolizumab should be omitted. It is currently unknown if the corticosteroid treatment reverses the gland dysfunction. Appropriate hormone replacement should also be initiated. Long-term hormone replacement therapy may be necessary.

Once symptoms or laboratory abnormalities are controlled and overall patient improvement is evident, treatment with pembrolizumab may be resumed and initiation of corticosteroid taper should be based on clinical judgment.

Hypophysitis can present as a diffuse, heterogenous enlargement of the pituitary on a brain MRI but can be completely normal. When hypophysitis with pituitary dysfunction is suspected, blood tests including thyroid stimulating hormone (TSH), free T4, adrenocorticotrophic stimulating hormone, cortisol, leutinizing hormone, and follicle-stimulating hormone should be obtained in women, and the first four plus testosterone in men. Typically the anterior pituitary axis is involved, affecting thyroid, gonadal, and adrenal function, but isolated axis dysfunction can be seen. Hypophysitis will cause low free T4 as well as TSH. Hypophysitis with clinically significant adrenal insufficiency and hypotension, dehydration, and electrolyte abnormalities such as hyponatremia and hyperkalemia constitutes adrenal crisis. Hospitalization and intravenous steroids with mineralocorticoid activity, such as methylprednisolone, should be initiated while waiting for laboratory results. Infection and sepsis should be ruled out with appropriate cultures and imaging. Prednisolone 1 mg/kg by mouth should be administered if patients are clinically stable. Steroids can usually be tapered over 30 days to achieve physiologic replacement levels. Thyroid hormone and/or testosterone replacement therapy may not be permanent, as the need for those hormones may wane over months in some patients. Cortisone replacement may also not be permanent in a modest portion of patients.

Eye

Uveitis is associated with pembrolizumab. All attempts should be made to rule out other causes such as metastatic disease, infection or other ocular disease (e.g. glaucoma or cataracts). For NCI-CTC grade 1-2 events evaluation by an ophthalmologist is recommended. Treatment with topical corticosteroids eye drops and iridocyclitics can be tried. Discontinue pembrolizumab if symptoms persist despite treatment with topical immunosuppressive therapy. Discontinue pembrolizumab for NCI-CTC grade 3 or above ocular symptoms and consider treatment with systemic corticosteroids. When symptoms improve to NCI-CTC grade 1 taper the corticosteroids over at least four weeks.

Gastrointestinal

Gastro-intestinal immune reactions include diarrhoea, increased frequency of bowel movements, abdominal pain or haematochezia, with or without fever. Diarrhoea or colitis occurring after initiation of pembrolizumab must be promptly evaluated to exclude infectious or other alternate causes. Immune-related colitis is often associated with evidence of mucosal inflammation, with or without ulcerations and lymphocytic and neutrophilic infiltration.

NCI-CTC grade 1 diarrhoea or suspected mild colitis may continue on pembrolizumab. Symptomatic treatment and close monitoring are advised.

For a NCI-CTC grade 2 – 3 colitis withhold the pembrolizumab and administer corticosteroids. Upon improvement to NCI-CTC grade 1 colitis begin to taper the corticosteroid over a period of one month. The pembrolizumab may be re-started when the colitis remains at NCI-CTC grade 1 following corticosteroid taper.

The pembrolizumab should be permanently discontinued when the colitis does not improve to at least NCI-CTC grade 1 within 12 weeks of the last dose, the corticosteroid dose cannot be reduced to 10mg or less of prednisolone or equivalent per day within 12 weeks or any NCI-CTC grade 3 or above reaction.

Lung

Interstitial lung disease including pneumonitis and acute interstitial pneumonitis are associated with pembrolizumab. For NCI-CTC grade 1 events (asymptomatic with radiographic findings only) then the pembrolizumab may be continued with close monitoring. Radiologic findings should be followed on serial imaging studies and consideration given to pulmonary consultation and/or bronchoscopy, if clinically indicated. For NCI-CTC grade 2 events withhold the pembrolizumab and consider pulmonary consultation with bronchoscopy and biopsy/bronchoalveolar lavage (BAL) and pulmonary function tests. Treat with systemic corticosteroids at a dose of 1 to 2 mg/kg/day prednisone or equivalent. When symptoms improve to NCI-CTC grade 1 or less, steroid taper should be started and continued over no less than 4 weeks. Treatment with pembrolizumab may be resumed if the event improves to NCI-CTC grade 0 or 1 within 12 weeks and corticosteroids have been reduced to the equivalent of prednisolone 10 mg oral daily or less. Repeat chest imaging monthly as clinically indicated.

Should a second episode of pneumonitis occur then discontinue pembrolizumab.

For NCI-CTC grade 3 or 4 events discontinue pembrolizumab and consider pulmonary function tests and seek advice from a lung specialist. A bronchoscopy with biopsy and / Or BAL should be considered. Treatment involves corticosteroid therapy such as intravenous methylprednisolone 125mg. When symptoms improve to NCI-CTC grade 1 or less, a high dose oral steroid such as prednisone 1 to 2 mg/kg once per day can be considered. A reducing schedule should be considered over a period of at least four weeks. If intravenous corticosteroids followed by high dose oral corticosteroids do not reduce initial symptoms within 48 to 72 hours, consider treatment with infliximab at 5 mg/kg once every 2 weeks. Discontinue infliximab upon symptom relief and initiate a prolonged steroid taper over 45 to 60 days. If symptoms worsen during steroid reduction, initiate a re-tapering of steroids starting at a higher

dose followed by a more prolonged taper and consider administration of infliximab. The decision to start infliximab should be made by a consultant.

Skin

Serious skin reactions include dermatitis exfoliative, erythema multiforme, Stevens-Johnson Syndrome and toxic epidermal necrolysis. Pembrolizumab can also be associated with pruritus, rash, (generalized and maculo-papular) and vitiligo. All attempts should be made to rule out other causes such as metastatic disease, infection or allergic dermatitis.

For NCI-CTC grade 1-2 skin reactions try symptomatic treatments such as topical corticosteroids or urea-containing creams in combination with oral antipruritics. Pembrolizumab can continue.

For NCI-CTC grade 3 or above events withhold the pembrolizumab and consider a dermatology referral. Treatment with systemic corticosteroids such as prednisolone 1mg/kg each day may be necessary. When symptoms improve to NCI-CTC grade 1 or less then steroid taper should be started and continued over no less than 4 weeks.

Regimen

The total duration of treatment is two years or 35 cycles. That is 4 cycles of combination chemotherapy with immunotherapy followed by 31 cycles of immunotherapy plus maintenance pemetrexed.

21 day cycle for 4 cycles

Drug	Dose	Days	Administration
Cisplatin	75mg/m ²	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/min (minimum time 120 minutes)
Pembrolizumab	200mg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes with a 0.2 micron filter
Pemetrexed	500mg/m ²	1	Intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes

| Followed by;

21 day cycle for 31 cycles

Drug	Dose	Days	Administration
Pembrolizumab	200mg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes with a 0.2 micron filter
Pemetrexed	500mg/m ²	1	Intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes

Dose Information

- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)
- Pemetrexed will be dose banded in accordance with the national dose bands (25NS)

Administration Information

- Cisplatin should be administered 30 minutes after the end of the pemetrexed infusion
- Pembrolizumab will be administered before the cisplatin and pemetrexed. It should be administered using a using a low protein binding filter.
- Pemetrexed may be administered in 100ml of either glucose 5% or sodium chloride 0.9% over 10 minutes. The choice of fluid will be dependant on the product stocked by pharmacy. The fluid and volume will not appear in the prescription but can be located in the instructions notepad.

Extravasation

- Cisplatin – exfoliant
- Pembrolizumab - neutral
- Pemetrexed - inflammitant

Additional Therapy

- Folic acid 5mg once daily starting 1 – 2 weeks prior to and continuing for three weeks after the last dose of pemetrexed.
- Hydroxocobalamin intramuscular injection 1mg every three months starting 1 – 2 weeks prior to pemetrexed.
- Antiemetics

15-30 minutes prior to chemotherapy (cycles 1, 2, 3, 4);

- aprepitant 125mg oral
- ondansetron 8mg oral or intravenous

As take home medication;

- aprepitant 80mg once a day oral for 2 days
- metoclopramide 10mg three times a day when required
- ondansetron 8mg twice a day for 3 days

Ensure the patient has taken the oral dexamethasone starting the day before pemetrexed. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg intravenous 15-30 minutes before chemotherapy.

As take home medication;

- dexamethasone 4mg twice a day oral for 3 days starting the day before chemotherapy is due.

15-30 minutes prior to chemotherapy (cycles 5-35)

- metoclopramide 10mg oral or intravenous

Ensure the patient has taken the oral dexamethasone starting the day before pemetrexed. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg intravenous 15-30 minutes before chemotherapy.

As take home medication;

- dexamethasone 4mg twice a day oral for 3 days starting the day before chemotherapy is due (not cycle 35)

- metoclopramide 10mg three times a day when required

- As required for the treatment of infusion related reactions (most common with pembrolizumab);

- chlorphenamine 10mg intravenous
- hydrocortisone 100mg intravenous
- paracetamol 1000mg oral

- Cisplatin pre and post hydration as follows;

Pre

Furosemide 40mg oral or intravenous

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Post

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed
- Prophylactic antibiotics can be considered if required

Additional Information

- Consideration should be given to draining pleural or peritoneal effusions prior to pemetrexed administration

Coding

- Procurement – X
- Delivery – X

References

1. Langer CJ, Gadgeel SM, Borghaei H et al. Carboplatin and pemetrexed with or without pembrolizumab for advanced non-squamous non small cell lung cancer: a randomised phase 2 cohort of the open label KEYNOTE 021 study. *Lancet Oncology* 2016; 17 (11): 1497-1508.

REGIMEN SUMMARY

Cisplatin-Pembrolizumab-Pemetrexed

Cycle 1, 2, 3, 4

Day Minus One

1. Dexamethasone 4mg twice a day oral*

Day One

2. Dexamethasone 4mg twice a day oral (from TTO)*
3. Aprepitant 125mg oral
4. Ondansetron 8mg oral or intravenous
5. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
Administration Instructions
Pembrolizumab should be administered using a low protein binding filter
6. Pemetrexed 500mg/m² intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
7. Furosemide 40mg oral or intravenous
8. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
9. Cisplatin 75mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)
Administration Instructions
Start 30 minutes after the end of the pemetrexed infusion.
10. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
11. Chlorphenamine 10mg intravenous when required for the treatment of infusion related reactions
12. Hydrocortisone sodium succinate 100mg intravenous when required for the treatment of infusion related reactions
13. Paracetamol 1000mg oral when required for the relief of infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines

14. Dexamethasone 4mg twice a day oral for 3 days starting the day before the pemetrexed infusion*
15. Aprepitant 80mg once a day oral for 2 days starting on day two of the cycle
16. Metoclopramide 10mg three times a day when required oral
17. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of the cycle
Administration Instructions
Start on the evening of day one of the cycle
18. Folic acid 5mg once a day oral

Cycle 5-34

Day Minus One

1. Dexamethasone 4mg twice a day oral*

Day One

2. Dexamethasone 4mg twice a day oral (from TTO)*
3. Metoclopramide 10mg oral or intravenous
4. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
Administration Instructions
Pembrolizumab should be administered using a low protein binding filter
5. Pemetrexed 500mg/m² intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
7. Chlorphenamine 10mg intravenous when required for the treatment of infusion related reactions
8. Hydrocortisone sodium succinate 100mg intravenous when required for the treatment of infusion related reactions
9. Paracetamol 1000mg oral when required for the relief of infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines

10. Dexamethasone 4mg twice a day oral for 3 days starting the day before the pemetrexed infusion*
11. Metoclopramide 10mg three times a day when required oral
12. Folic acid 5mg once a day oral

Cycle 35

Day Minus One

1. Dexamethasone 4mg twice a day oral*

Day One

2. Dexamethasone 4mg twice a day oral (from TTO)*
3. Metoclopramide 10mg oral or intravenous
4. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
Administration Instructions
Pembrolizumab should be administered using a low protein binding filter
5. Pemetrexed 500mg/m² intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
7. Chlorphenamine 10mg intravenous when required for the treatment of infusion related reactions
8. Hydrocortisone sodium succinate 100mg intravenous when required for the treatment of infusion related reactions
9. Paracetamol 1000mg oral when required for the relief of infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines

11. Metoclopramide 10mg three times a day when required oral
12. Folic acid 5mg once a day oral

Hydroxocobalamin will not be included as part of the Aria regime and must be prescribed separately on the cycle for which it is due.

* In Aria Planner the dexamethasone 4mg twice daily will appear on days 1, 2, 3 of treatment. This is the supply for the next cycle. The patient should have been given the supply for cycle one in the pre-assessment or consent clinic. The administration instructions reflect this.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	February 2019	None	Dr Deborah Wright Pharmacist	Dr Judith Cave Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
 NHS Isle of Wight
 Portsmouth Hospitals NHS Trust
 Salisbury Hospitals NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.