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Thames Valley Chemotherapy Regimens

Lung Cancer

Notes from the editor

All chemotherapy regimens, and associated guidelines eg antiemetics and dose bands are available on the Network website **www.tvscn.nhs.uk/networks/cancer-topics/chemotherapy/**

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Acknowledgements
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Thames Valley Chemotherapy Regimens

Lung Cancer

Network Chemotherapy regimens used in the management of Lung Cancer
Date published: June 2018
Date of review: June 2020

Chemotherapy Regimens

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List of amendments in this version

Regimen type: Lung Tumours
Date due for review: June 2020
Previous Version number: 3.9
This version number: 4.0

Table 1 Amendments

Page	Amendment	Made/ asked by
	Diluent volume amendments as per national dose standardisation spoecifications	

Table 2 New regimens to be approved and checked by PODG included in this version

Name of regimen	Indication	Reason / Proposer
Atezolizumab	NSCLC	CDF

For anti-emetic guidelines: http://tvscn.nhs.uk/networks/cancer/cancer-topics/chemotherapy/

For dose banded chemotherapy standardized product specifications: www.england.nhs.uk/commissioning/spec-services/npc-crg/group-b/b02/dose-banded-chemotherapy-standardised-product-specifications/

ACE (SCLC)

Indication: Has been used as first line treatment for SCLC but platinum/etoposide is preferred

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

DRUG REGIMEN

Day 1 **DOXORUBICIN** 40mg/^{2} IV bolus
CYCLOPHOSPHAMIDE 600mg/m^2 IV bolus
ETOPOSIDE 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
Day 2 **ETOPOSIDE** 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
Day 3 **ETOPOSIDE** 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
*doses 48mg to 88mg in 250ml, doses 96mg to 180mg in 500ml sodium chloride 0.9%

NB Day 2 and 3 etoposide can be given orally ETOPOSIDE 200mg/m^2 PO but is not recommended as oral absorption is variable (it may cause reduced efficacy or severe toxicity in patients), the intravenous route is preferred, however for logistical reasons the oral route may be necessary.

Cycle Frequency: Every 21 days
Number of cycles: Usually 6 (subject to tolerance and response)

DOSE MODIFICATIONS

Doxorubicin:
Dose reduce in severe renal impairment.
Bilirubin 20-50micromol/L give 50% dose
Bilirubin 51-85micromol/L give 25% dose
Bilirubin >85micromol/L omit
If AST is 2-3 x ULN give 75% dose
If AST is >3 x ULN give 50% dose

Maximum cumulative dose = 450 mg/m^2 (in normal cardiac function)
= 400 mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

Etoposide:
CrCl >50ml/min give 100% dose
CrCl 15-50ml/min give 75% dose
CrCl <15ml/min give 50% dose
Bilirubin 26-51micromol/L or AST 60-180u/L give 50% dose
Bilirubin >51micromol/L or AST >180u/L Clinical decision

Cyclophosphamide:
GFR >20ml/min give 100% dose
GFR 10-20ml/min give 75% dose
GFR <10ml/min give 50% dose

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFT)
Serum Creatinine

2) Non urgent blood tests
Tests relating to disease response/progression
ECG (possibly ECHO) required if patient has preexisting cardiac disease (Doxorubicin)

CONCURRENT MEDICATION

ANTIEMETIC POLICY

High emetic risk day 1
Low emetic risk days 2 and 3

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Cyclophosphamide may irritate bladder, drink copious volumes of water.
Cardiotoxicity – Monitor cardiac function to minimise the risk of anthracycline induced cardiac failure. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.

REFERENCES

1. Aisner J *et al.* Cancer Treat Rep 1982; 66: 221 230
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

CAV (SCLC)

Indication: First line treatment for SCLC in patients not able to tolerate platinum and etoposide (e.g. performance status of 3). Can also be used as second line treatment after relapse.

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

DRUG REGIMEN

Day 1 **VINCRISTINE** 1.3mg/m^2 (max. 2 mg) in 50ml sodium chloride 0.9% IV over 10 mins
DOXORUBICIN 40mg/m^2 IV bolus
CYCLOPHOSPHAMIDE 750 mg/m^2 IV bolus

Cycle Frequency: Every 21 days
Number of cycles: Usually 6 (subject to tolerance and response)

DOSE MODIFICATIONS

Vincristine:
If patient complains of tingling of fingers and/or toes, discuss.
Bilirubin 25-51micromol/L or AST 60-180u/L give 50% dose
Bilirubin >51micromol/L and normal AST give 50% dose
Bilirubin >51micromol/L and AST >180u/L omit

Doxorubicin:
Dose reduce in severe renal impairment.
Bilirubin 20-50micromol/L give 50% dose
Bilirubin 51-85micromol/L give 25% dose
Bilirubin >85micromol/L omit
If AST is 2-3 x ULN give 75% dose
If AST is >3 x ULN give 50% dose

Maximum cumulative dose = 450 mg/m^2 (in normal cardiac function)
= 400 mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

Cyclophosphamide:
GFR >20ml/min give 100% dose
GFR 10-20ml/min give 75% dose
GFR <10ml/min give 50% dose

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFT)
Serum Creatinine

2) Non urgent blood tests
Tests relating to disease response/progression ECG (possibly ECHO) required if patients has pre-existing cardiac disease (Doxorubicin)

CONCURRENT MEDICATION

ANTIEMETIC POLICY

High emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Cardiotoxicity – Monitor cardiac function to minimise the risk of anthracycline induced cardiac failure. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Cyclophosphamide may irritate bladder, drink copious volumes of water.

REFERENCES

1. Greco FA *et al.* Am J Med 1979; 66: 625 630.
2. Roth BJ *et al.* J Clin Oncol 1992; 10: 282291
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

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Carboplatin Etoposide (SCLC)

Indication: Standard first line treatment for SCLC

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

DRUG REGIMEN

Day 1 **CARBOPLATIN** AUC 5 infusion in 500ml glucose 5% infusion over 60 minutes
Dose (mg) = AUC x (GFR+25)
ETOPOSIDE 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
Day 2 **ETOPOSIDE** 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
Day 3 **ETOPOSIDE** 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
***doses 48mg to 88mg in 250ml, doses 96mg to 180mg in 500ml sodium chloride 0.9%

NB Day 2 and 3 can be given orally ETOPOSIDE 100mg/bd PO but is not recommended as oral absorption is variable (it may cause reduced efficacy or severe toxicity in patients), the intravenous route is preferred, however for logistical reasons the oral route may be necessary. If days 2 and 3 are given orally the day 1 IV dose should be increased to 120mg/m^2.

Ideally EDTA GFR should be used,

Cycle Frequency: Every 21 days
Number of cycles: Usually 6 (subject to tolerance and response)

DOSE MODIFICATIONS

Carboplatin:
Discuss if patient has a serum creatinine > 150 micromol/L
If GFR / calculated CrCl = or < 20ml/min contraindicated.

Etoposide:
CrCl >50ml/min give 100% dose
CrCl 15-50ml/min give 75% dose
CrCl <15ml/min give 50% dose
Bilirubin 26-51micromol/L or AST 60-180u/L give 50% dose
Bilirubin >51micromol/L or AST >180u/L Clinical decision

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Ideally EDTA GFR should be used (Carboplatin) Creatinine clearance (GFR) calculated, at the Consultants discretion
Liver function tests (LFT)

2) Non urgent blood tests. Tests relating to disease response/progression

CONCURRENT MEDICATION FOR PREVENTION

Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously.
DEXAMETHASONE 20mg IV bolus
CHLORPHENAMINE 10mg IV bolus
RANITIDINE 50mg IV bolus
Carboplatin should be given at a slower rate e.g. 2-4 hours.

ANTIEMETIC POLICY

Moderate emetic risk day 1
Low emetic risk days 2 and 3

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Ototoxicity - monitor
Neurotoxicity – monitor.

REFERENCES

1. Skarlos DV *et al.* Ann Oncol 1994; 5: 601 607
2. Daniels, S. and S. Gabriel, Dosage adjustment for cytotoxics in renal impairment and hepatic impairment. 2009, The North London Cancer Network.
3. Study 12/14

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Cisplatin (75) Etoposide (100) (SCLC)

Indication: Standard first line treatment for SCLC at ORH with concurrent radiotherapy

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

DRUG REGIMEN

Day 1 Pre-hydration
ETOPOSIDE 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
CISPLATIN 75mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours
Post hydration
Day 2 **ETOPOSIDE** 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
Day 3 **ETOPOSIDE** 100mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
*doses 48mg to 88mg in 250ml, doses 96mg to 180mg in 500ml sodium chloride 0.9%

NB Day 2 and 3 etoposide can be given orally ETOPOSIDE 200mg/m^2/day but is not recommended as oral absorption is variable (it may cause reduced efficacy or severe toxicity in patients), the intravenous route is preferred, however for logistical reasons the oral route may be necessary.

Cycle Frequency: Every 21 days
Number of cycles: Usually 6 (subject to tolerance and response)

DOSE MODIFICATIONS

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR <45ml/min omit dose

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Etoposide:
CrCl >50ml/min give 100% dose
CrCl 15-50ml/min give 75% dose
CrCl <15ml/min give 50% dose
Bilirubin 26-51micromol/L or AST 60-180u/L give 50% dose
Bilirubin >51micromol/L or AST >180u/L Clinical decision

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated, or EDTA at the Consultants discretion (Cisplatin)
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.

ANTIEMETIC POLICY

High emetic risk day 1
Low emetic risk days 2 and 3

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

1. Evans WK *et al.* J Clin Oncol 1985; 3: 1471 1477. Roth BJ *et al.* J Clin Oncol 1992; 10: 282291
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

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Cisplatin (60) with Etoposide (120) (SCLC)

Indication: Standard first line treatment for SCLC at RBH and HWP

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

DRUG REGIMEN

Day 1 Pre-hydration
ETOPOSIDE 120mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
CISPLATIN 60mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours
Post-hydration
Day 2 **ETOPOSIDE** 120mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
Day 3 **ETOPOSIDE** 120mg/m^2 infusion in 1000ml* sodium chloride 0.9% over 60 minutes
*doses 48mg to 88mg in 250ml, doses 96mg to 180mg in 500ml sodium chloride 0.9%

NB Day 2 and 3 etoposide can be given orally ETOPOSIDE 240mg/m^2/day but is not recommended as oral absorption is variable (it may cause reduced efficacy or severe toxicity in patients), the intravenous route is preferred, however for logistical reasons the oral route may be necessary.

Cycle Frequency: Every 21 days
Number of cycles: Usually 6 (subject to tolerance and response)

DOSE MODIFICATIONS

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR <45ml/min consider carboplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration

Etoposide:
CrCl >50ml/min give 100% dose
CrCl 15-50ml/min give 75% dose
CrCl <15ml/min give 50% dose
Bilirubin 26-51micromol/L or AST 60-180u/L give 50% dose
Bilirubin >51micromol/L or AST >180u/L Clinical decision

INVESTIGATIONS

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated, or EDTA at the Consultants discretion (Cisplatin)
Liver function tests (LFT)

2) Non urgent blood tests: tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.

ANTIEMETIC POLICY

High emetic risk day 1
Low emetic risk days 2 and 3

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

1. Evans WK *et al.* J Clin Oncol 1985; 3: 1471 1477.
2. Roth BJ *et al.* J Clin Oncol 1992; 10: 282291
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

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TOPOTECAN (oral) (SCLC)

Indication: Relapsed small cell lung cancer (second line)

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

NICE: Oral topotecan is recommended as an option only for people with relapsed small-cell lung cancer for whom re-treatment with the first-line regimen is not considered appropriate **and** the combination of cyclophosphamide, doxorubicin and vincristine (CAV) is contraindicated (for details of the contraindications to CAV see the summary of product characteristics for each of the component drugs).

DRUG REGIMEN
Days 1 to 5 Topotecan 2.3mg/m^2 orally daily

Cycle Frequency: Every 3 weeks until progression

DOSE MODIFICATIONS

Topotecan:
Renal impairment
CrCl >40ml/min give 100% dose
CrCl 20-39ml/min give 50% dose
CrCl <20ml/min contraindicated

Hepatic impairment
Bilirubin <170micromol/L give 100% dose
Bilirubin >170micromol/L Clinical decision
Neutropenia
Standard oncology practice for the management of neutropenia is either to administer topotecan with other medications (e.g. G-CSF) or to dose reduce to maintain neutrophil counts. In this clinical situation, dose reduction is usually appropriate
If dose reduction is chosen for patients who experience severe neutropenia (neutrophil count < 0.5 x 10^9/l) for seven days or more, or severe neutropenia associated with fever or infection, or who have had treatment delayed due to neutropenia, the dose should be reduced by 0.4 mg/m^2/day to 1.9 mg/m^2/day (or subsequently down to 1.5 mg/m^2/day if necessary).

INVESTIGATIONS

Routine Blood test

1) Blood results required before drug administration

	Give	*Discuss*
Hb x g/dL	9	< 9
Plt x 10^9/L	100	< 100
Neutrophils x 10^9/L	1.5	< 1.5 1st treatment, <1.0 for subsequent treatment

Creatinine

Liver function tests (LFT)

2) Non urgent blood tests

Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Febrile neutropenia

Interstitial lung disease

Diarrhoea - may be severe and on occasion associated with neutropenic colitis. It should be managed aggressively with anti-diarrhoeals, antibiotics, maintenance of hydration and admission if required.

REFERENCES

1. NICE TA 184 November 2009
2. SPC November 2010

AFATINIB (NSCLC)

Indication: Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation-positive locally advanced or metastatic Non Small Cell Lung Cancer where the person has not previously had an EGFR-TK inhibitor

NICE TA310 Afatinib is recommended as a possible treatment for adults with locally advanced or metastatic non-small-cell lung cancer if: their cancer tests positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation and they have not had a type of drug called an EGFR-TK inhibitor before

DRUG REGIMEN

Day 1 **Afatinib** 40mg orally daily (may be escalated to 50mg/daily)

Cycle Frequency: Until disease progression or unacceptable toxicity.
Review every 2 months by CT scan

DOSE MODIFICATIONS

If dose reduction required reduce dose by 10mg increments to 20mg

Afatinib:
Renal impairment
Severe renal impairment (CrCl <30ml/min) not recommended.

Hepatic impairment
Exposure to afatinib is not significantly changed in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. Adjustments to the starting dose are not necessary in patients with mild or moderate hepatic impairment. This medicinal product has not been studied in patients with severe (Child Pugh C) hepatic impairment. Treatment in this population is not recommended

INVESTIGATIONS

Routine Blood test

1) Blood results required before drug administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Blood tests should initially be performed 4 weekly, but later in the treatment course can be done less often in stable patients.

Creatinine
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Take one hour before or two hours after meals.
Some of the following may be required for treatment of the skin rash:
E45 / Diprobase,
Hydrocortisone 1%/2.5%,
Clindamycin gel 1%,
Oxytetracycline 500mg po bd (for 2 weeks)
Prednisolone 25mg po od for 7 days then reducing by 5mg per day to stop.

ANTIEMETIC POLICY

Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Skin rash – initial rash may be severe.
Diarrhoea –Proactive management of diarrhoea including adequate hydration combined with anti-diarrhoeal medicinal products especially within the first 6 weeks of the treatment is important and should start at first signs of diarrhoea.

REFERENCES

Afatinib Named Patient Use (1200.52) Information Pack Sept 2011
SPC June 2014

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ATEZOLIZUMAB (NSCLC)

Indications: Atezolizumab for treating previously platinum-treated locally advanced/ metastatic non squamous or squamous non-small cell lung cancer which has been prospectively determined before this application to be PD-L1 positive or PD-L1 negative or PD-L1 unquantifiable at PD-L1 assay or one in which PD-L1 status cannot be determined on account of insufficient lung cancer tissue being available for PD-L1 assay
2. The prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.
3. The patient has a histologically- or cytologically-confirmed diagnosis of stage IIIB or IV non-small cell lung cancer and is either non-squamous or squamous in type.
4. The patient has either progressed after previously receiving at least 2 cycles of platinum-containing chemotherapy for stage IIIB or IV non-small cell lung cancer and also a targeted treatment if the tumour is EGFR positive or ALK positive or progressed within 6 months of completing platinum-based chemotherapy given as adjuvant or neoadjuvant therapy or concurrent with radiotherapy
5. PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score (TPS) has been attempted prior to this application. Either:- The TPS score will be documented- The TPS score cannot be documented as the TPS result was unquantifiable - PD-L1 testing was not possible as the pathologist has documented that there is insufficient tissue for PD-L1 analysis
6. The patient has a performance status (PS) of 0 or 1 and would otherwise be potentially fit for docetaxel-based 2nd line chemotherapy
7. The patient has no symptomatically active brain metastases or leptomeningeal metastases.
8. Atezolizumab will be administered as monotherapy
9. 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
10. Atezolizumab will be stopped at 2 years of treatment or on loss of clinical benefit or unacceptable toxicity, whichever occurs first.
11. A formal medical review as to whether treatment with atezolizumab should continue or not will be scheduled to occur at least by the end of the first 9 weeks of treatment
12. Treatment breaks of up to 12 weeks beyond the expected cycle length of atezolizumab are allowed solely to allow immune toxicities to settle
13. Atezolizumab will otherwise be used as set out in SPC with the exception of criteria 10

DRUG REGIMEN

Day 1 **Atezolizumab** 1200mg in 250ml sodium chloride 0.9% IV infusion

Cycle Frequency: every 3 weeks until disease progression to a maximum 2 years

DOSE MODIFICATIONS

Dose modification advice for specified adverse drug reactions

Pneumonitis	
Grade 2	Withhold Atezolizumab Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day
≤Grade 3 or 4	Permanently discontinue Atezolizumab
Hepatitis	
Grade 2: (ALT or AST > 3 to x ULN or bilirubin > 1.5 to 3 x ULN)	Withhold Atezolizumab Treatment may be resumed when the event improves to Grade 0 or 5 x [ULN]x Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ or blood 10 mg prednisone or equivalent per day
Grade 3 or 4: (ALT or AST > 5 x ULN or blood bilirubin > 3 x ULN)	Permanently discontinue Atezolizumab
Colitis	
Grade 2 or 3 Diarrhoea (increase of ≥ 4 stools/day over baseline) or Symptomatic Colitis	Withhold Atezolizumab Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisone equivalent per day
Grade 4 Diarrhoea or Colitis (life threatening; urgent intervention indicated)	Permanently discontinue Atezolizumab
Hypothyroidism or hyperthyroidism	
Symptomatic	Withhold Atezolizumab Hypothyroidism: Treatment may be resumed when symptoms are controlled by thyroid replacement therapy and TSH levels are decreasing Hyperthyroidism: Treatment may be resumed when symptoms are controlled by antithyroid medicinal product and thyroid function is improving

Adrenal insufficiency	
Symptomatic	Withhold Atezolizumab Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day and patient is stable on replacement therapy
Hypophysitis	
Grade 2 or 3	Withhold Atezolizumab Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day and patient is stable on replacement therapy
Grade 4	Permanently discontinue Atezolizumab
Type 1 diabetes mellitus	
Grade 3 or 4 hyperglycaemia (fasting glucose > 250 mg/dL or 13.9 mmol/L)	Withhold Atezolizumab Treatment may be resumed when metabolic control is achieved on insulin replacement therapy
Infusion-related reactions	
Grade 1 or 2	Reduce infusion rate or interrupt. Treatment may be resumed when the event is resolved
Grade 3 or 4	Permanently discontinue Atezolizumab
Rash	
Grade 3	Withhold Atezolizumab Treatment may be resumed when rash is resolved and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day
Grade 4	Permanently discontinue Atezolizumab
Myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome and Meningoencephalitis	
All Grades	Permanently discontinue Atezolizumab

Pancreatitis	
Grade 3 or 4 serum amylase or lipase levels increased (> 2 x ULN) or Grade 2 or 3 pancreatitis	Withhold Atezolizumab Treatment may be resumed when serum amylase and lipase levels improve to Grade 0 or Grade 1 within 12 weeks, or symptoms of pancreatitis have resolved, and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day
Grade 4 or any grade of recurrent pancreatitis	Permanently discontinue Atezolizumab

Atezolizumab should be permanently discontinued:
• For Grade 4 toxicities except for endocrinopathies that are controlled with replacement hormones
• For any recurrent event at Grade ≥ 3 severity
• If a treatment-related toxicity does not resolve to Grade 0 or Grade 1 within 12 weeks after adverse reaction onset date
• If a corticosteroid dose of > 10 mg prednisone or equivalent per day is required for treatment-related toxicity beyond 12 weeks after adverse reaction onset date.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated or EDTA at the Consultants discretion (Cisplatin)

2) Non-urgent tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

None required

ANTI-EMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

inflammation of the lung (pneumonitis): symptoms may include new or worsening cough, shortness of breath, and chest pain
• inflammation of the liver (hepatitis): symptoms may include yellowing of skin or eyes, nausea, vomiting, bleeding or bruising, dark urine, and stomach pain
• inflammation of the intestines (colitis): symptoms may include diarrhoea (watery, loose or soft stools), blood in stools, and stomach pain
• inflammation of the thyroid and adrenal glands (hypo-thyroidism, hyper-thyroidism, or adrenal insufficiency): symptoms may include tiredness, weight loss, weight gain, change in mood, hair loss, constipation, and dizziness
• type 1 diabetes mellitus, including acid in the blood produced from diabetes (diabetic ketoacidosis): symptoms may include feeling more hungry or thirsty than usual, need to urinate more often, weight loss, and feeling tired
• inflammation of the brain (encephalitis) or inflammation of the membrane around the spinal cord and brain (meningitis): symptoms may include neck stiffness, headache, fever, chills, vomiting, eye sensitivity to light, confusion and sleepiness
• inflammation or problems of the nerves (neuropathy): symptoms may include muscle weakness and numbness, tingling in hands and feet
• inflammation of the pancreas (pancreatitis): symptoms may include abdominal pain, nausea and vomiting
• severe reactions associated with infusion (events occurring during or within one day of having the infusion) may include fever, chills, shortness of breath and flushing.

REFERENCES

SPC

CERITINIB (NSCLC)

***Indication:* Treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.**

The first line treatment of anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer
2. The patient has a histologically or cytologically confirmed diagnosis of stage IIIB or IV non small cell lung cancer that carries an anaplastic lymphoma kinase (ALK) rearrangement
3. The patient has received no previous ALK-targeted therapy
4. The patient has received no previous cytotoxic chemotherapy for locally advanced or metastatic non small cell lung cancer ie no previous systemic treatment except when this has been given as neoadjuvant or adjuvant therapy or concurrently with radiotherapy
5. Ceritinib will be used only as single-agent therapy
6. The patient has an ECOG performance status of 0 or 1 or 2
7. The patient either has no brain metastases or, if the patient has brain metastases, the patient is symptomatically stable prior to starting ceritinib
8. The patient will be treated until loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment, whichever is the sooner
9. Treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle
10. Ceritinib will be otherwise used as set out in its Summary of Product Characteristics
11. Crizotinib is to be used only if the patient cannot tolerate ceritinib and has not had progressive disease whilst on ceritinib. Crizotinib is not to be used following disease progression on ceritinib as there is no current clear evidence to support treatment with crizotinib after disease progression on ceritinib

NICE TA395 Ceritinib is recommended, within its marketing authorisation, as an option for treating advanced anaplastic lymphoma kinase positive non-small-cell lung cancer in adults who have previously had crizotinib. The drug is recommended only if the company provides it with the discount agreed in the patient access scheme.

DRUG REGIMEN

Day 1 **Ceritinib** 450mg orally daily (with or after food)

Cycle Frequency: Until disease progression or unacceptable toxicity.
Review every 2 months by CT scan

DOSE MODIFICATIONS

Dose Interruption, Reduction, or Discontinuation Recommendations

ALT or AST elevation greater than 5 times ULN with total bilirubin elevation less than or equal to 2 times ULN

Withhold until recovery to baseline or less than or equal to 3 times ULN, then resume ceritinib with a 150mg dose reduction.

ALT or AST elevation greater than 3 times ULN with total bilirubin elevation greater than 2 times ULN in the absence of cholestasis or hemolysis

Permanently discontinue ceritinib.

Any Grade treatment-related ILD/pneumonitis

Permanently discontinue ceritinib.

QTc interval greater than 500 msec on at least 2 separate ECGs

Withhold until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then resume ceritinib with a 150mg dose reduction.

QTc interval prolongation in combination with Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia

Permanently discontinue ceritinib.

Severe or intolerable nausea, vomiting or diarrhea despite optimal anti-emetic or anti-diarrheal therapy

Withhold until improved, then resume ceritinib. with a 150mg dose reduction.

Persistent hyperglycemia greater than 250 mg/dL despite optimal anti-hyperglycemic therapy

Withhold until hyperglycemia is adequately controlled, then resume ceritinib with a 150mg dose reduction.

If adequate hyperglycemic control cannot be achieved with optimal medical management, discontinue ceritinib.

Symptomatic bradycardia that is not life-threatening

Withhold until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, evaluate concomitant medications known to cause bradycardia, and adjust the dose of ceritinib.

Clinically significant bradycardia requiring intervention or life-threatening bradycardia in patients taking a concomitant medication also known to cause bradycardia or a medication known to cause hypotension

Withhold until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above.

If the concomitant medication can be adjusted or discontinued, resume ceritinib. with a 150mg dose reduction, with frequent monitoring.

Life-threatening bradycardia in patients who are not taking a concomitant medication also known to cause bradycardia or known to cause hypotension

Permanently discontinue ceritinib..

Dose Modification for Strong CYP3A4 Inhibitors

Avoid concurrent use of strong CYP3A inhibitors during treatment with ceritinib If concomitant use of a strong CYP3A inhibitor is unavoidable, reduce the ceritinib dose by a pproximately one-third, rounded to the nearest 150 mg dosage strength. After discontinuation of a strong CYP3A inhibitor, resume the ceritinib dose that was taken prior to initiating the strong CYP3A4 inhibitor.

INVESTIGATIONS

Pre assessment
CT- chest abdomen pelvis
FBC
U and E's
LFT's
ECG
Creatinine

Blood tests should initially be performed monthly
FBC
Creatinine
Liver function tests (LFT)

CONCURRENT MEDICATION

ANTIEMETIC POLICY

Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

REFERENCES

SPC September 2015

June 2018June 2020

NHS
Thames Valley

Cisplatin (50) Etoposide (50) with RT (NSCLC)

Indication: Superior sulcus non-small cell carcinoma

DRUG REGIMEN

Day 1, 8, 29 & 36 Pre-hydration
CISPLATIN 50mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours
Post hydration
Days 1 to 5 **ETOPOSIDE** 50mg/m^2 infusion in 500ml* sodium chloride 0.9% over 60 minutes
Days 29 to 33 **ETOPOSIDE** 50mg/m^2 infusion in 500ml* sodium chloride 0.9% over 60 minutes
*doses 48mg to 88mg in 250ml, 96mg to 180mg in 500ml, 200mg to 360mg in 1000ml sodium chloride 0.9%

This regimen is given concurrently with radiotherapy. Radiation and chemotherapy to start within 24 hours of each other.

Number of cycles: 1 cycle

DOSE MODIFICATIONS

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR < 45ml/min consider carboplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Etoposide:
CrCl >50ml/min give 100% dose
CrCl 15-50ml/min give 75% dose
CrCl <15ml/min give 50% dose
Bilirubin 26-51micromol/L or AST 60-180u/L give 50% dose
Bilirubin >51micromol/L or AST >180u/L Clinical decision

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated or EDTA at the Consultants discretion (Cisplatin)
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.

ANTIEMETIC POLICY

High emetic risk days 1, 8, 29 and 36
Low emetic risk days 2 to 5 and days 30 to 33

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

1. Rusch VW, Giroux KJ, Kraut JC et al. Induction Chemoradiation and Surgical Resection for Superior Sulcus Non-Small Cell Lung Carcinomas: Long-Term Results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160). J Clin Oncol 25: 313-318, 2007.

NHS
Thames Valley

Cisplatin Vinorelbine with concurrent RT (NSCLC)

Indication: Non-small cell lung cancer suitable for chemoradiotherapy

DRUG REGIMEN

Days 1 to 4 & 22 to 25 Pre-hydration
CISPLATIN 20mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours (with fractions 1-4 and 16-19 of radiotherapy)
Post hydration

Days 1, 8, 19 & 26 **VINORELBINE** 15mg/m^2 infusion in 50ml sodium chloride 0.9% over 10 minutes prior to radiotherapy on fractions 1, 6, 15, and 20

Radiotherapy should be given no more than 6 hours after starting the cisplatin

Number of cycles: 1 cycle of 42 days

DOSE MODIFICATIONS

Haematological

ANC X109/L		PLATELETS X109/L	VINORELBINE	CISPLATIN
>1.5	and	>100	100%	100%
1.0-1.5	or	60-100	omit	100%
<1.0	or	<60	omit	omit

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR < 45ml/min consider carboplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Vinorelbine:
If bilirubin > 2 x ULN or AST/ALT > 5 x ULN reduce to 66.6%

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated or EDTA at the Consultants discretion (Cisplatin)
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.
Ciprofloxacin 500mg po BD days 8 to 20 and 29 to 41

ANTIEMETIC POLICY

Highly emetogenic day 1-4 and 22-25
Minimal emetogenic risk days 8, 19 and 26

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

SOCCAR trial

NHS
Thames Valley

GEMCITABINE CISPLATIN (NSCLC)

Indication: Standard combination for palliative treatment of NSCLC
Unknown primary if appropriate

NICE guidance – www.nice.org.uk
Docetaxel, gemcitabine, paclitaxel and vinorelbine should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.

DRUG REGIMEN

Day 1 PRE-HYDRATION
GEMCITABINE 1250mg/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes
CISPLATIN 80mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours
POST-HYDRATION
Day 8 **GEMCITABINE** 1250mg/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes

Cycle Frequency: Every 21 days
Number of cycles: up to 4 (subject to tolerance and response)

DOSE MODIFICATIONS

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR < 45ml/min consider carboplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Gemcitabine:
CrCl <30ml/min consider dose reduction (Clinical decision)
If bilirubin >27micromol/L initiate treatment with dose of 800mg/m^2

Neutrophils >1.5x10x^9/L and platelets >100x10x^9/L give 100% dose (Day 1 and 8)
Neutrophils 0.5-1.5x10x^9/L or platelets 50-100x10x^9/L give 75% dose (Day 8 only) or delay based on clinical assessment (Day 1 and 8)
Neutrophils <0.5x10x^9/L or platelets <50x10x^9/L delay treatment (Day 1) or omit treatment (Day 8).

Diarrhoea and/or mucositis
Grade 2 toxicity – omit until toxicity resolved then restart at 100% dose
Grade 3 toxicity – omit until toxicity resolved then restart at 75% dose
Grade 4 toxicity – omit until toxicity resolved then restart at 50% dose

Omit if treatment is delayed for more than 4 weeks but continue with Cisplatin

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFT)

Creatinine clearance (GFR) calculated OR EDTA at the Consultants discretion (Cisplatin).

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.

ANTIEMETIC POLICY

High emetic risk day 1
Low emetic risk day 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Diarrhoea – see dose modifications treat with loperamide or codeine.
Mucositis – see dose modifications use routine mouth care.

REFERENCES

1. Giaccone G *et al.* Seminars in Oncology 2002; 29 (3) Supp 9: 47 49
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

CISPLATIN (40) concurrent radiotherapy (NSCLC)

Indication: Unresectable stage IIIA/IIIB Non small cell lung cancer concurrently with radical radiotherapy after neoadjuvant chemotherapy with 2 cycles of cisplatin/vinorelbine.

DRUG REGIMEN

Day 1 Pre-hydration

CISPLATIN 40mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours

Post-hydration

Cycle Frequency: Every week for 4 weeks. Start early in Radiotherapy.

DOSE MODIFICATIONS

Cisplatin:

GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR < 45ml/min consider carboplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated, or EDTA at the Consultants discretion. (Cisplatin)
Consider transfusions to keep Hb > 12 x g/dL

2) Non urgent blood tests Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.

ANTIEMETIC POLICY

Moderately emetic risk.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

1. SchaakeKoning C *et al.* N Eng J Med 1992; 326: 524 530
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

CRIZOTINIB (NSCLC)

Indications:
Crizotinib for untreated anaplastic lymphoma kinase-positive advanced NSCLC
2. The patient has a histologically or cytologically conformed diagnosis of stage IIIB or IV non smallcell lung cancer that carries an anaplastic lymphoma kinase (ALK) rearrangement
3. The patient has had no previous 1st line systemic therapy (chemotherapy or other ALK inhibitors) for advanced or metastatic non-small cell lung cancer unless any NICE-approved 1st line ALK inhibitor therapy has had to be discontinued on account of unacceptable toxicity AND there is no evidence of disease progression
4. The patient will receive the licensed dose and frequency of crizotinib.

Crizotinib for previously treated anaplastic lymphoma kinase-positive advanced NSCLC
2. The patient has a histologically or cytologically conformed diagnosis of stage IIIB or IV nonsmallcell lung cancer that carries an anaplastic lymphoma kinase (ALK) rearrangement
3. This is a 2nd or subsequent line treatment post 1st line platinum based combination chemotherapy and the patient has not previously been treated with another ALK inhibitor
3. The patient will receive crizotinib as set out in its SPC

First or subsequent line systemic therapy for ROS1-positive inoperable locally advanced/metastatic non squamous NSCLC
Histologically or cytologically non-squamous NSCLC (stage IIIB or stage IV) with a confirmed ROS1 gene rearrangement as demonstrated by an accurate and validated assay. The patient has received no previous ROS1-targeted therapy.
EITHER the patient has received no previous cytotoxic chemotherapy for locally advanced or metastatic non-small cell lung cancer OR has been previously treated with cytotoxic chemotherapy for locally advanced or metastatic disease Note: NHS England has a strong preference for ROS1-positive patients to be treated with crizotinib as 1st line therapy for locally advanced/metastatic NSCLC, though recognises that some patients have had to be treated with chemotherapy for urgent clinical reasons before the ROS1 result was known
No brain metastases or, if the patient has brain metastases, the patient is symptomatically stable prior to starting crizotinib. ECOG performance status of 0 or 1 or 2.
Crizotinib will be otherwise used as set out in its SPC

DRUG REGIMEN

Day 1 **Crizotinib** 250mg orally twice daily

Cycle Frequency: Continuously until disease progression

DOSE MODIFICATIONS

Renal impairment
No starting dose adjustment is recommended for patients with mild (creatinine clearance 60 to 90 mL/min) and moderate renal impairment (CLcr 30 to 60 mL/min). No data are available in patients with severe and end-stage renal disease and, no formal dosing recommendation could be made.

Hepatic impairment
Clinical studies that were conducted excluded patients with AST or ALT >2.5 x upper limit of normal (ULN), or if due to underlying malignancy, >5.0 x ULN or with total bilirubin >1.5 x ULN. Treatment with Crizotinib should be used with caution in patients with mild and moderate hepatic impairment and should not be used in patients with severe hepatic impairment,

CTCAE grade	Treatment
Grade 3 or 4 alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevation with Grade ≤1 total bilirubin	Withhold until recovery to Grade ≤1 or baseline, then resume at 200 mg twice daily[b]
Grade 2, 3 or 4 ALT or AST elevation with concurrent Grade 2, 3 or 4 total bilirubin elevation (in the absence of cholestasis or hemolysis)	Permanently discontinue
Any Grade pneumonitis[c]	Permanently discontinue
Grade 3 QTc prolongation	Withhold until recovery to Grade ≤1, then resume at 200 mg twice daily[b]
Grade 4 QTc prolongation	Permanently discontinue

INVESTIGATIONS

Routine Blood test
1) Blood results required before drug administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Blood tests should initially be performed 4 weekly, but later in the treatment course can be done less often in stable patients.
Creatinine
Liver function tests (LFT)
2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY

Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

REFERENCES

DOCETAXEL (75) (NSCLC)

Indication:
Second line therapy for NSCLC after failure of platinum containing chemotherapy

NICE guidance www.nice.org.uk
Docetaxel monotherapy should be considered where second line treatment is appropriate for patients with locally advanced or metastatic NSCLC when relapse has occurred after prior chemotherapy.

DRUG REGIMEN

Day 1 PREMEDICATION: **DEXAMETHASONE** 8 mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)
DOCETAXEL 75mg/m^2 infusion in 250ml sodium chloride 0.9% over 60 minutes

Cycle Frequency: Every 21 days

Number of cycles: Individualised but not usually more than 6 (subject to tolerance and response)

DOSE MODIFICATIONS

Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure pre-medication is given.
This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions

ANTIEMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

REFERENCES

1. Shepherd F *et al.* J Clin Oncol 2000; 18: 2095 2103. Fossella F *et al.* J Clin Oncol 2000; 18: 2354 2362
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

DOCETAXEL (75) CISPLATIN (75) (NSCLC)

Indication: First line therapy for NSCLC

NICE guidance www.nice.org.uk
Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.

DRUG REGIMEN

Day 1 PREMEDICATION: **DEXAMETHASONE** 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)
Pre-hydration
DOCETAXEL 75mg/m^2 in 250ml sodium chloride 0.9% over 60 minutes
CISPLATIN 75mg/m^2 in 1000ml sodium chloride 0.9% infusion over 2 hours
Post-hydration

Cycle Frequency: Every 21 days
Number of cycles: 4 to 6 cycles

DOSE MODIFICATIONS

Docetaxel:
Discuss if severe cutaneous reactions,
peripheral neuropathy or fluid retention after previous course.
Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR <45ml/min consider carboplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated OR EDTA at the Consultants discretion.

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Docetaxel - Ensure pre-medication is given.
This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions
Cisplatin - Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.

ANTIEMETIC POLICY

High emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Docetaxel - Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.
Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.

REFERENCES

1. Shepherd F *et al.* J Clin Oncol 2000; 18: 2095 2103.
2. Fossella F *et al.* J Clin Oncol 2000; 18: 2354 2362
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

DOCETAXEL (75) CARBOPLATIN (NSCLC)

Indication: First line therapy for NSCLC

NICE guidance www.nice.org.uk
Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.

DRUG REGIMEN

Day 1 PREMEDICATION: **DEXAMETHASONE** 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)
DOCETAXEL 75mg/m^2 in 250ml sodium chloride 0.9% over 60 minutes
CARBOPLATIN AUC5 in 500ml glucose 5% infusion over 60 minutes

Cycle Frequency: Every 21 days
Number of cycles: 4 to 6 cycles

DOSE MODIFICATIONS

Docetaxel:
Discuss if severe cutaneous reactions,
peripheral neuropathy or fluid retention after previous course.

Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

Carboplatin:
Discuss if patient has a serum creatinine > 150 micromol/L
If EDTA GFR = or < 20ml/min contraindicated

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) EDTA at the Consultants discretion.

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Docetaxel - Ensure pre-medication is given.
This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions
Ototoxicity - monitor
Neurotoxicity – monitor.

ANTIEMETIC POLICY

Moderate emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Docetaxel - Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.
Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.

REFERENCES

1. Shepherd F *et al.* J Clin Oncol 2000; 18: 2095 2103.
2. Fossella F *et al.* J Clin Oncol 2000; 18: 2354 2362
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

ERLOTINIB (NSCLC)

Indication: Locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen.
Factors associated with prolonged survival should be taken into account when prescribing erlotinib.

NICE TA162 Erlotinib is recommended as an alternative to docetaxel for patients with non-small-cell lung cancer (NSCLC) who have already tried one chemotherapy regimen but it has not worked. Erlotinib should be used only when the manufacturer provides the drug at the same overall treatment cost as docetaxel. This cost includes the cost of giving the drug, treatments for any side effects and the cost of monitoring patients to check that treatment is working.

NICE recommends erlotinib as a possible first-line treatment (that is, if you have not had drug treatment before) for some people with locally advanced or metastatic non-small-cell lung cancer.

DRUG REGIMEN

Day 1 **Erlotinib** 150mg orally daily

Cycle Frequency: Initial review after 1 or 2 weeks of treatment then review every month until stable then review every 2 months

DOSE MODIFICATIONS

If dose reduction required reduce dose to 100mg daily

Erlotinib:
Renal impairment
Severe renal impairment - erlotinib not recommended.

Hepatic impairment
Mild – moderate hepatic impairment – dose reduction or interruption of erlotinib should be considered if severe adverse reactions occur.
Severe hepatic impairment – erlotinib not recommended

INVESTIGATIONS

Routine Blood test

1) Blood results required before drug administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Blood tests should initially be performed 4 weekly, but later in the treatment course can be done less often in stable patients.

Creatinine
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Take one hour before or two hours after meals.
Some of the following may be required for treatment of the skin rash:
E45 / Diprobase,
Hydrocortisone 1%/2.5%,
Clindamycin gel 1%,
Oxytetracycline 500mg po bd (for 2 weeks)
Prednisolone 25mg po od for 7 days then reducing by 5mg per day to stop.

ANTIEMETIC POLICY

Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Skin rash – initial rash may be severe.
Diarrhoea – dose reduction may be required. Moderate or severe diarrhoea may require loperamide

REFERENCES

1. Erlotinib in previously treated non-small cell lung cancer. Shepherd FA, Pereira JR, Ciuleanu, T et al. N Engl J Med 2005;353; 123-132

GEFITINIB (NSCLC)

Indication: Locally advanced or metastatic non-small cell lung cancer, first line

NICE: Gefitinib is recommended as an option for the first-line treatment of people with locally advanced or metastatic non-small-cell lung cancer (NSCLC) if: they test positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation.

DRUG REGIMEN

Day 1 **Gefitinib** 250mg orally daily

Cycle Frequency: Continuous treatment

DOSE MODIFICATIONS

Gefitinib:

Renal imparment
CrCl ≤20ml/min caution is advised

Hepatic impairment
Patients with moderate to severe hepatic impairment due to cirrhosis have increased plasma concentrations of gefitinib. These patients should be closely monitored for adverse events. Plasma concentrations were not increased in patients with elevated aspartate transaminase (AST), alkaline phosphatase or bilirubin due to liver metastases.

INVESTIGATIONS

Routine Blood test
1) Blood results required before drug administration

	Give	*Discuss*
Hb x g/dL	10	< 10
Plt x 10^9/L	100	< 100
Neutrophils x 10^9/L	1.5	< 1.5

Blood tests should initially be performed 4 weekly, but later in the treatment course can be done less often in stable patients.

Creatinine
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Take at the same time each day. Swallow whole or disperse tablets in half a glass of water (noncarbonated) without crushing it. The glass should be swirled occasionally, until the tablet is dispersed (this may take up to 20 minutes). The dispersion should be drunk immediately after dispersion is complete (i.e. within 60 minutes). The glass should be rinsed with half a glass of water, which should also be drunk.

ANTIEMETIC POLICY

Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Skin rash
Diarrhoea
Elevation in ALT

REFERENCES

1. Gefitinib SPC July 2009
2. NICE TA 192 July 2010

NHS
Thames Valley

GEMCITABINE (1200) CARBOPLATIN (NSCLC and SCLC)

Indication: Standard combination for palliative treatment of NSCLC / SCLC
Unknown primary if appropriate

NICE guidance www.nice.org.uk
Docetaxel, gemcitabine, paclitaxel and vinorelbine should each be considered, with a platinum drug, as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.

People with small-cell lung cancer should have treatment initiated within 2 weeks of the pathological diagnosis. (NICE)

DRUG REGIMEN

Day 1 GEMCITABINE 1200mg/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes
CARBOPLATIN AUC 5* infusion in 500ml glucose 5% over 30-60 minutes
Dose = (25 + GFR) x AUC
Day 8 GEMCITABINE 1200mg/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes

Cycle Frequency: Every 21 days
Number of cycles: Up to 4 for NSCLC and up to 6 for SCLC (subject to tolerance and response)

NB * EDTA GFR should be used, If GFR is measured or EDTA then: AUC = 5
If calculated from serum creatinine the result is less accurate

DOSE MODIFICATIONS

Carboplatin:
Discuss if patient has a serum creatinine > 150 micromol/L
If GFR/ calculated CrCl = or < 20ml/min contraindicated

Gemcitabine:
CrCl <30ml/min consider dose reduction (Clinical decision)
If bilirubin >27micromol/L initiate treatment with dose of 800mg/m2
Neutrophils >1.5x10x9/L and platelets >100x10x9/L give 100% dose (Day 1 and 8)
Neutrophils 0.5-1.5x10x9/L or platelets 50-100x10x9/L give 75% dose (Day 8 only) or delay based on clinical assessment (Day 1 and 8)
Neutrophils <0.5x10x9/L or platelets <50x10x9/L delay treatment (Day 1) or omit treatment (Day 8).

Diarrhoea and/or mucositis
Grade 2 toxicity – omit until toxicity resolved then restart at 100% dose
Grade 3 toxicity – omit until toxicity resolved then restart at 75% dose
Grade 4 toxicity – omit until toxicity resolved then restart at 50% dose

Omit if treatment is delayed for more than 4 weeks but continue with Carboplatin

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFTs)

GFR should be measured using EDTA clearance. Estimating creatinine clearance from the serum creatinine, weight and age is less accurate.

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously.
DEXAMETHASONE 20mg IV bolus
CHLORPHENAMINE 10mg IV bolus
RANITIDINE 50mg IV bolus
Carboplatin should be given at a slower rate e.g. 2-4 hours.

ANTIEMETIC POLICY

Moderate emetic risk day 1
Low emetic risk day 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Diarrhoea – see dose modifications treat with loperamide or codeine.
Mucositis – see dose modifications use routine mouth care.
Ototoxicity - monitor
Neurotoxicity – monitor

REFERENCES

1. Danson S *et al.* Cancer 2003; 98: 542 553
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

GEMCITABINE (NSCLC)

Indication: Palliative treatment of NSCLC when patient not fit enough to tolerate platinum (e.g. performance status 2)

NICE guidance – www.nice.org.uk
Docetaxel, gemcitabine, paclitaxel and vinorelbine should each be considered as part of firstline chemotherapy options for advanced (stage III and IV) NSCLC patients.

DRUG REGIMEN

Day 1 GEMCITABINE 1g/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes
Day 8 GEMCITABINE 1g/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes
Day 15 GEMCITABINE 1g/m^2 infusion in 250ml sodium chloride 0.9% over 30 minutes

Cycle Frequency: Every 28 days
Number of cycles: Up to 4 (subject to tolerance and response)

DOSE MODIFICATIONS

CrCl <30ml/min consider dose reduction (Clinical decision)
If bilirubin >27micromol/L initiate treatment with dose of 800mg/m2

Neutrophils >1.5x10x^9/L and platelets >100x10x^9/L give 100% dose (Day 1 and 8)
Neutrophils 0.5-1.5x10x^9/L or platelets 50-100x10x^9/L give 75% dose (Day 8 only) or delay based on clinical assessment (Day 1 and 8)
Neutrophils <0.5x10x^9/L or platelets <50x10x^9/L delay treatment (Day 1) or omit treatment (Day 8).

Diarrhoea and/or mucositis
Grade 2 toxicity – omit until toxicity resolved then restart at 100% dose
Grade 3 toxicity – omit until toxicity resolved then restart at 75% dose
Grade 4 toxicity – omit until toxicity resolved then restart at 50% dose

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent blood tests.
Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Diarrhoea – see dose modifications treat with loperamide or codeine.
Mucositis – see dose modifications use routine mouth care.

REFERENCES

1. Gridelli C *et al.* Journal of the National Cancer Institute 2003; 95: 363 372
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NINTEDANIB DOCETAXEL (NSCLC)

Indication: Previously treated locally advanced, metastatic, or locally recurrent NSCLC

NICE guidance www.nice.org.uk
TA347 for treating locally advanced, metastatic or locally recurrent non-small-cell lung cancer of adenocarcinoma histology that has progressed after first-line chemotherapy.

DRUG REGIMEN

Day 1 PREMEDICATION: **DEXAMETHASONE** 8mg BD starting 24 hours before chemotherapy or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)
DOCETAXEL 75mg/m^2 infusion in 250ml sodium chloride 0.9% over 60 minutes
Days 2-21NINTEDANIB 200mg bd PO

Cycle Frequency: Every 21 days. Following completion of at least 4 cycles (up to 6 cycles) of docetaxel and nintedanib combination, nintedanib may continue as monotherapy until disease progression

DOSE MODIFICATIONS

Docetaxel
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

Nintedanib
As initial measure for the management of adverse reactions treatment with nintedanib should be temporarily interrupted until the specific adverse reaction has resolved to levels that allow continuation of therapy (to grade 1 or baseline).
Nintedanib treatment may be resumed at a reduced dose. Dose adjustments in 100mg steps per day (ie a 50mg reduction per dosing) based on individual safety and tolerability are recommended as below.
In case of further persistence of the adverse reaction(s), ie if a patient does not tolerate 100mg twice daily, treatment with nintedanib should be permanently discontinued. In case of specific elevations of aspartate aminotransferase (AST)/ alanine aminotransferase (ALT) values to >3xULN in conjunction with an increase of total bilirubin to ≥ 2 x ULN and alkaline phosphatase (ALKP) <2xULN; (see below) treatment with nintedanib should be interrupted. Unless there is an alternative cause established, nintedanib should be permanently discontinued.
Recommended dose adjustments for nintedanib in case of diarrhoea, vomiting and other nonhaematological or haematological adverse reactions

CTCAE* Adverse reaction	Dose adjustment
Diarrhoea ≥ grade 2 for more than 7 consecutive days despite anti-diarrhoeal treatment ***OR*** Diarrhoea ≥ grade 3 despite anti-diarrhoeal treatment Vomiting ≥ grade 2 daily. ***AND/OR*** Nausea ≥ grade 3 despite anti-emetic treatment Other non-haematological or haematological adverse reaction of ≥ grade 3	After treatment interruption and recovery grade 1 or baseline, dose reduction from 200mg twice daily to 150mg twice daily and - if a 2nd dose reduction is considered necessary - from 150mg twice daily to 100mg twice daily

Recommended dose adjustments for nintedanib in case of AST and/or ALT and bilirubin elevations

AST / ALT and bilirubin elevations	Dose adjustment
Elevation of AST and/or ALT values to > 2.5 x ULN in conjunction with total bilirubin elevation to ≥ 1.5 x ULN ***OR*** Elevation of AST and/or ALT values to > 5x ULN	After treatment interruption and recovery of transaminase-values to ≤ 2.5x ULN in conjunction with bilirubin to normal, dose reduction from 200mg twice daily to 150mg twice daily and - if a 2nd dose reduction is considered necessary - from 150mg twice daily to 100mg twice daily.
Elevation of AST and/or ALT values to > 3 x ULN in conjunction with an increase of total bilirubin to ≥ 2 x ULN and ALKP < 2 x ULN	Unless there is an alternative cause established, nintedanib should be permanently discontinued

The docetaxel dose can be reduced, only once, as follows:
• from 75mg/m^2 to 60mg/m^2
• patients that require a second docetaxel reduction and have not completed a minimum of 4 cycles of combination therapy should be discontinued. Those that have completed 4 cycles may continue to receive nintedanib monotherapy.
In some cases treatment should be temporarily interrupted, to allow for the adverse event to recover to CTCAE Grade: = <1 or baseline before re-starting at a reduced dose.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure pre-medication is given.
This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions
Loperamide may be required.

ANTIEMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.
Diarrhoea, nausea and vomiting
Venous thromboembolic events

REFERENCES

1. Shepherd F *et al.* J Clin Oncol 2000; 18: 2095 2103. Fossella F *et al.* J Clin Oncol 2000; 18: 2354 2362
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NIVOLUMAB

Indications:
The treatment of previously treated locally advanced or metastatic non-squamous non-small-cell lung cancer
2. The patient has a confirmed diagnosis of stage IIIB or IV non-squamous non-small cell lung cancer
3. The patient has progressed after previously receiving at least 2 cycles of platinum-containing chemotherapy for stage IIIB or IV non-small cell lung cancer and also a targeted treatment if the tumour is EGFR positive or ALK positive
4. The patient has an ECOG performance status of 0 or 1
5. 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 unless it was received as part of the nivolumab EAMS programme for this indication and the patient meets all other criteria listed here
6. The patient has had PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score.
7. The patient's tumour expresses PD-L1 (that is, with a tumour proportion score (TPS) ≥ 1%) by an approved and validated test.
8. The patient's tumour proportion score* is: * Note: the patient's TPS score must be provided, otherwise the application will not be authorised.
9. Nivolumab will be administered as monotherapy.
10. The patient has no symptomatically active brain metastases or leptomeningeal metastases.
11. Nivolumab will be stopped at 2 years of treatment or on disease progression* or unacceptable toxicity, whichever occurs first.*Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until further disease progression is confirmed.
12. Nivolumab will otherwise be used as set out in its SPC with the exception of criterion 11.

The treatment of previously treated locally advanced or metastatic squamous non-small-cell lung cancer
3. The patient has a histologically or cytologically confirmed diagnosis of stage IIIB or IV squamous non-small cell lung cancer.
4. The patient has progressed after previously receiving at least 2 cycles of platinum-containing chemotherapy for stage IIIB or IV non-small cell lung cancer and also a targeted treatment if the tumour is EGFR positive or ALK positive.
5. The patient has an ECOG performance status of 0 or 1 and would otherwise be potentially fit for docetaxel-based 2nd line chemotherapy.
6. 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 unless it was received as part of the nivolumab EAMS programme for this indication and the patient meets all other criteria listed here.

7. Every effort has been made for the patient to have PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score (TPS). Please document the TPS results below:- TPS (if negative enter zero): OR- Please enter 'yes', if the TPS cannot be quantified OR- Please enter 'yes', if PD-L1 testing was not possible as the pathologist has documented that these was insufficient tissue
8. Nivolumab will be administered as monotherapy.
9. The patient has no symptomatically active brain metastases or leptomeningeal metastases.
10. Nivolumab will be stopped at 2 years of treatment or on disease progression* or unacceptable toxicity, whichever occurs first.*Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until further disease progression is confirmed.
11. Nivolumab will otherwise be used as set out in its SPC with the exception of criterion 11.

Blueteq form needs to be completed for all patients for all funding streams

DRUG REGIMEN

Day 1 **NIVOLUMAB** 240mgin 100ml* sodium chloride 0.9% infusion over 30 minutes

Cycle Frequency: Every 14 days until progression or intolerance (maximum 2 years)

DOSE MODIFICATIONS

Nivolumab:

Renal impairment

Based on the population pharmacokinetic (PK) results, no dose adjustment is required in patients with mild or moderate renal impairment. Data from patients with severe renal impairment are too limited to draw conclusions on this population.

Hepatic impairment

Based on the population PK results, no dose adjustment is required in patients with mild hepatic impairment. Data from patients with moderate or severe hepatic impairment are too limited to draw conclusions on these populations. Nivolumab must be administered with caution in patients with moderate (total bilirubin > 1.5 × to 3 × the upper limit of normal [ULN] and any AST) or severe (total bilirubin > 3 × ULN and any AST) hepatic impairment.

Immune-related adverse reaction	Severity	Treatment modification
Immune-related pneumonitis	Grade 2 pneumonitis	Withhold dose(s) until symptoms resolve, radiographic abnormalities improve, and management with corticosteroids is complete
	Grade 3 or 4 pneumonitis	Permanently discontinue treatment
Immune-related colitis	Grade 2 diarrhoea or colitis	Withhold dose(s) until symptoms resolve and management with corticosteroids, if needed, is complete
	Grade 3 diarrhoea or colitis - Nivolumab monotherapy	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete
	Grade 4 diarrhoea or colitis	Permanently discontinue treatment
Immune-related hepatitis	Grade 2 elevation in aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin	Withhold dose(s) until laboratory values return to baseline and management with corticosteroids, if needed, is complete
	Grade 3 or 4 elevation in AST, ALT, or total bilirubin	Permanently discontinue treatment
Immune-related nephritis and renal dysfunction	Grade 2 or 3 creatinine elevation	Withhold dose(s) until creatinine returns to baseline and management with corticosteroids is complete
	Grade 4 creatinine elevation	Permanently discontinue treatment
Immune-related endocrinopathies	Symptomatic Grade 2 or 3 hypothyroidism, hyperthyroidism, hypophysitis, Grade 2 adrenal insufficiency Grade 3 diabetes	Withhold dose(s) until symptoms resolve and management with corticosteroids (if needed for symptoms of acute inflammation) is complete. Treatment should be continued in the presence of hormone replacement therapy[a] as long as no symptoms are present
	Grade 4 hypothyroidism Grade 4 hyperthyroidism Grade 4 hypophysitis Grade 3 or 4 adrenal insufficiency Grade 4 diabetes	Permanently discontinue treatment
	Grade 4 rash	Permanently discontinue treatment
Other adverse reactions	Grade 3 (first occurrence)	Withhold dose(s)
	Grade 4 or recurrent Grade 3 ; persistent Grade 2 or 3 despite treatment modification ; inability to reduce corticosteroid dose to 10 mg prednisone or equivalent per day	Permanently discontinue treatment

INVESTIGATIONS

Routine Blood test
1) Blood results required before drug administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY

None required

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.
Immune-mediated adverse reactions: Administer corticosteroids based on the severity of the reaction.
- Immune-mediated pneumonitis: Withhold for moderate and permanently iscontinue for severe or life-threatening pneumonitis.
- Immune-mediated colitis: Withhold for moderate or severe and permanently discontinue for life-threatening colitis.
- Immune-mediated hepatitis: Monitor for changes in liver function. Withhold for moderate and permanently discontinue for severe or lifethreatening transaminase or total bilirubin elevation.
- Immune-mediated nephritis and renal dysfunction: Monitor for changes in renal function. Withhold for moderate and permanently discontinue for severe or life-threatening serum creatinine elevation.
- Immune-mediated hypothyroidism and hyperthyroidism: Monitor for changes in thyroid function. Initiate thyroid hormone replacement as needed.
- Embryofetal toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception.

REFERENCES

1. SPC Nivolumab SPC Ref 3677021 June 2015
2. CDF October 2017

OSIMERTINIB (NSCLC)

***Indication:* The treatment of locally advanced or metastatic epidermal growth factor receptor and T790M mutation-positive non-small-cell lung cancer (NSCLC) where all the following criteria are met:**
-Histologically or cytologically documented NSCLC that carries an EGFR and a T790M mutation
-Locally advanced or metastatic NSCLC.
-Radiological documentation of disease progression following 1st line EGFR TKI treatment with only one TKI and without any further systemic anticancer treatment.
-Treatment with no more than one prior line of treatment for advanced NSCLC.
-No prior chemotherapy unless any prior neoadjuvant or adjuvant chemotherapy had been completed at least 6 months prior to starting 1st line EGFR treatment.
-PS 0 or 1
-At time of starting osimertinib, the patient must be fit enough to have potentially started platinum-based doublet chemotherapy

DRUG REGIMEN

Day 1 **Osimertinib 80**mg orally daily

Cycle Frequency: continuously until disease progression or unacceptable toxicity

DOSE MODIFICATIONS

Osimertinib:
Renal impairment
No recommended dose in severe renal impairment (CrCl<30ml/min) or end stage renal disease.

Hepatic impairment
No recommended dose in moderate /severe hepatic impairment.

PULMONARY
- Interstitial lung disease /pneumonitis - discontinue permanently

CARDIAC
QTc interval >500msec on at least 2 separate occasions- withold until interval <481 or recovery to baseline if baseline > 481 msec then resume at 40mg
QTC prolongation with signs/symptoms of life threatening arrhythmia - discontinue permanently
Asymptomatic, absolute decrease in LVEF of 10% from baseline and below 50% - withhold for up to 4 weeks- if improved to baseline LVEF , resume. If not improved to baseline - discontinue permanently.
Symptomatic congestive heart failure- discontinue permanently

OTHER
Grade 3 or higher adverse reaction – withhold for up to 3 weeks
If improvement to grade 0-2 within 3 weeks - Resume at 80 or 40mg daily
If no improvement within 3 weeks- discontinue permanently

INVESTIGATIONS

PRE - ASSESSMENT
lung function tests, FBC, full biochemistry, chest xray ECG (repeat ECG after 2 weeks of treatment)

MONTHLY
FBC, full biochemistry, Creatinine, Liver function tests (LFT) (ECG for patients with ongoing risk of other QT prolonging medication or cardiac failure)

Blood tests should initially be performed 4 weekly, but later in the treatment course can be done less often in stable patients.

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Some of the following may be required for treatment of the skin rash:
E45 / Diprobase,
Hydrocortisone 1%/2.5%,
Clindamycin gel 1%,
Oxytetracycline 500mg po bd (for 2 weeks)
Prednisolone 25mg po od for 7 days then reducing by 5mg per day to stop

ANTIEMETIC POLICY

Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Skin rash – initial rash may be severe.
Diarrhoea – dose reduction may be required. Moderate or severe diarrhoea may require loperamide
Interstitial lung disease/pneumonitis
Cardiomyopathy
QTc interval prolongation

REFERENCES

New England Journal Of Medicine Pasi A et all Vol 372 No 18 pages 1689-1699

NHS
Thames Valley

PACLITAXEL 80mg (days 1, 8 and 15)

Indication: NSCLC

DRUG REGIMEN

Day 1 PREMEDICATION 30mins prior to infusion:
DEXAMETHASONE 8mg IV bolus
RANITIDINE 50mg IV bolus
CHLORPHENAMINE 10mg IV bolus
PACLITAXEL 80mg/m^2 in 250ml* sodium chloride 0.9% infusion over 1 hour
*doses 162mg to 600mg in 500ml sodium chloride 0.9%

Cycle Frequency: Days 1, 8 and 15 every 28 days up to 3 cycles subject to tolerance and response

DOSE MODIFICATIONS

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration.

In the absence of Gilbert's syndrome:
Bilirubin >51micromol/L stop treatment

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure pre-medication is given.

ANTIEMETIC POLICY

Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

(2% risk of severe hypersensitivity)

Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision.
If further reactions occur stop treatment.

PEMBROLIZUMAB (1st line)

Indication: The treatment of untreated PD-L1 positive metastatic non-small-cell lung cancer where all the following criteria are met:
2. The prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.
3. The patient has a histologically- or cytologically-confirmed diagnosis of stage IIIB or IV non-small cell lung cancer (squamous or non-squamous)
4. The patient's tumour expresses PD-L1 (that is, with a tumour proportion score [TPS] ≥50%) by an approved and validated test
5. The patient either does not have an adenocarcinoma/non-squamous histology OR does have an adenocarcinoma/non-squamous histology but does not have an EGFR or ALK-positive tumour.
6. The patient has not received previous systemic therapy for advanced /metastatic disease. Completion of treatment with CT and/or RT as part of neoadj/adj therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of metastatic disease
7. The patient has a performance status (PS) of 0 or 1 and is potentially fit for platinum-based chemotherapy
8. The patient has no active brain metastases or leptomeningeal metastases
9. Pembrolizumab will be administered as monotherapy
10. The patient has not received prior treatment with an anti-PD-1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody unless received as part of the pembrolizumab EAMS programme for this indication and meeting all other criteria listed.
11. Pembrolizumab will be stopped at 2 years of treatment or on disease progression* or unacceptable toxicity, whichever occurs first.
****Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until further disease progression is confirmed.***
12. Pembrolizumab will be used as outlined in the SPC with the exception of criteria 11

DRUG REGIMEN

Day 1 **PEMBROLIZUMAB** 200mg in 100ml sodium chloride 0.9% infusion over 30 minutes

Cycle Frequency: Every 21 days until disease progression for a maximum of 2 years uninterrupted treatment

DOSE MODIFICATIONS

Pembrolizumab
See Immuno-oncology adverse event management guidelines

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration
FBC,U&Es including magnesium, ,Cr, LFTs Every cycle
TFT Every other cycle
ECG
Non urgent blood tests - Tests relating to disease response/progression

CONCURRENT MEDICATION

None required.

ANTIEMETIC POLICY

Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Immune-mediated pneumonitis
Immune-mediated colitis
Immune-mediated hepatitis
Immune-mediated endocrinopathies

REFERENCES

SPC July 2015
CDF May 2017

PEMBROLIZUMAB (following previous treatment)

Indication: The treatment of PD-L1-positive non small-cell lung cancer after chemotherapy where all the following criteria are met:
The prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.
The patient has a histologically- or cytologically-confirmed diagnosis of stage IIIB or IV non-small cell lung cancer (squamous or non-squamous).
The patient's tumour expresses PD-L1 (that is, with a tumour proportion score [TPS] ≥1%) by an approved and validated test.
The patient has progressed after treatment with at least two cycles of platinum-containing doublet chemotherapy for stage IIIB/IV disease AND a targeted treatment if they have an EGFR or ALK-positive tumour.
The patient has an ECOG performance status of 0 or 1.
The patient has no active brain metastases or leptomeningeal metastases.
The patient has not received prior treatment with an anti-PD-1, anti-PDL2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.
Pembrolizumab will be stopped at 2 years of treatment or on disease progression* or unacceptable toxicity, whichever occurs first.
****Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until further disease progression is confirmed.***

DRUG REGIMEN

Day 1 **PEMBROLIZUMAB** 2mg/kg in 100ml* sodium chloride 0.9% infusion over 30 minutes
*doses 80mg to 100mg in 50ml sodium chloride 0.9%

Cycle Frequency: Every 21 days until disease progression for a maximum of 2 years

DOSE MODIFICATIONS

Pembrolizumab
See Immuno-oncology adverse event management guidelines

INVESTIGATIONS

Routine Blood test
2) Blood results required before chemotherapy administration
FBC,U&Es including magnesium, ,Cr, LFTs Every cycle
TFT Every other cycle
ECG
Non urgent blood tests - Tests relating to disease response/progression

CONCURRENT MEDICATION
None required.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Immune-mediated pneumonitis
Immune-mediated colitis
Immune-mediated hepatitis
Immune-mediated endocrinopathies

REFERENCES
SPC July 2015

VINORELBINE (25) CARBOPLATIN (NSCLC)

Indication: Palliative treatment of NSCLC.

NICE guidance www.nice.org.uk Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.

DRUG REGIMEN

Day 1 **VINORELBINE** 25mg/m^2 in 50ml sodium chloride 0.9% IV infusion over 10 mins
CARBOPLATIN AUC = 5* in 500ml glucose 5% over 1 hour
Dose = (25 + GFR) x AUC
Day 8 **VINORELBINE** 25mg/m^2 in 50ml sodium chloride 0.9% IV infusion over 10 mins

Cycle Frequency: Every 21 days
Number of cycles: 2 or 3 if given in neoadjuvant and adjuvant setting, up to 4 in palliative setting (subject to tolerance and response)

NB *Ideally EDTA GFR should be used, If GFR is measured or EDTA then: AUC = 5
If calculated from serum creatinine the result is less accurate

DOSE MODIFICATIONS

Previous neutropenic sepsis, discuss with Consultant or Registrar

Vinorelbine:
If there is significant hepatic impairment the dose should be reduced
If bilirubin > 2 x ULN and AST/ALT >5 x ULN give 66.6% dose

Carboplatin:
Discuss if patient has a serum creatinine > 150 micromol/L
If GFR/ calculated CrCl = or < 20ml/min contraindicated

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

GFR should be measured using EDTA clearance. Estimating creatinine clearance from the serum creatinine, weight and age is less accurate.
Liver function tests (LFTs)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously.
DEXAMETHASONE 20mg IV bolus
CHLORPHENAMINE 10mg IV bolus
RANITIDINE 50mg IV bolus
Carboplatin should be given at a slower rate e.g. 2-4 hours.

ANTIEMETIC POLICY

Moderate emetic risk day 1
Minimal emetic risk day 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Ototoxicity - monitor
Neurotoxicity – monitor

REFERENCES

1. Baldini E *et al.* Br J Cancer 1998; 77: 2367 2370.
2. Cremonesi M *et al.* Oncology 2003; 64 : 97-101
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

VINORELBINE (25) CISPLATIN (80) (NSCLC)

Indication: Palliative treatment of unresectable NCSLC.
Also used as neoadjuvant treatment prior to radical chemoradiotherapy and adjuvant treatment of patients following complete resection of non-small cell lung cancer

NICE guidance www.nice.org.uk. Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.
4 cycles of vinorelbine plus cisplatin are indicated for adjuvant treatment of patients following complete resection of non small cell lung cancer

DRUG REGIMEN

Day 1 Pre-hydration
VINORELBINE 25mg/m^2 in 50ml sodium chloride 0.9% IV infusion over 10 mins
CISPLATIN 80mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours
Post-hydration
Day 8 **VINORELBINE** 25mg/m^2 in 50ml sodium chloride 0.9% IV infusion over 10 mins

Cycle Frequency: Every 21 days
Number of cycles: 2 or 3 if given in neoadjuvant and adjuvant setting, up to 4 in palliative setting (subject to tolerance and response)

DOSE MODIFICATIONS

Vinorelbine:
If there is significant hepatic impairment the dose should be reduced
If bilirubin > 2 x ULN and AST/ALT >5 x ULN give 66.6% dose

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR <45ml/min consider carboplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated OR EDTA at the Consultants discretion (Cisplatin).
Liver function tests (LFTs)

2) Non urgent blood tests.
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure adequate pre and post hydration prescribed as per day case schedule at the end of TVCN regimens.
If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.
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ANTIEMETIC POLICY

High emetic risk day 1
Minimal emetic risk day 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

1. Wozniak AJ *et al.* J Clin Oncol 1998; 16: 2459 2465
2. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

VINORELBINE (NSCLC)

NICE guidance – www.nice.org.uk
Docetaxel, gemcitabine, paclitaxel and vinorelbine should each be considered as part of first-line chemotherapy options for advanced (stage III and IV) NSCLC patients.

Indication: Palliative treatment of NSCLC when patient not fit enough to tolerate platinum (e.g. performance status 2)

DRUG REGIMEN

Day 1 VINORELBINE 30mg/m^2 in 50ml sodium chloride 0.9% IV infusion over 10 mins
Day 8 VINORELBINE 30mg/m^2 in 50ml sodium chloride 0.9% IV infusion over 10 mins

Administration should always be followed by a 250ml sodium chloride 0.9% infusion to flush the vein.

Cycle Frequency: Every 21 days
Number of cycles: Individualised but rarely more than 4

DOSE MODIFICATIONS

If there is significant hepatic impairment the dose should be reduced
If bilirubin > 2 x ULN and AST/ALT >5 x ULN give 66.6% dose

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent blood tests - Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY

Minimal emetic risk.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

REFERENCES

1. Gridelli C *et al.* Oncologist 2001; 6: Supp 1: 4 7

VINORELBINE (oral) (NSCLC)

***Indication:* Palliative treatment of stage III or IV NSCLC or patients not fit enough to tolerate platinum**

NICE guidance www.nice.org.uk. Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.
4 cycles of vinorelbine plus cisplatin are indicated for adjuvant treatment of patients following complete resection of non-small cell lung cancer

DRUG REGIMEN

Cycle 1
Day 1, 8 and 15 **VINORELBINE** 60mg/m^2 orally once a week. (Maximum dose 160 mg/week)

Cycle 2 onwards - dose escalation at the Consultant's discretion if cycle 1 tolerated
Day 1, 8 and 15 **VINORELBINE** 80mg/m^2 orally once a week (see dose modifications)
(Maximum dose 160 mg/week)

NB capsules should be swallowed with food and water without chewing or sucking the capsule at least 30 minutes after antiemetic. Available as 20, 30, 40 and 80mg capsules
NB Based on clinical studies, the oral dose of 80 mg/m^2 was demonstrated to correspond to 30 mg/m^2 of the iv form and 60 mg/m^2 to 25 mg/m^2

Cycle Frequency: every 21 days

DOSE MODIFICATIONS AND DELAYS

Dose escalation from cycle 2 onwards to 80mg/m^2 except in patients for whom the neutrophil count has dropped once below 0.5 x10^9/L OR more than once between 0.5-1.0 x10^9/L during the first cycle doses, in these patients continue at 60mg/m^2

For doses planned to be given at 80mg/m², if the neutrophil count is below 0.5 x10^9/L OR more than once between 0.5-1.0 x10^9/L administration should be delayed until recovery and the dose reduced from 80 to 60mg/m^2 per week during the following cycles.

If the neutrophil count is below 1.5 x10^9/L AND/OR the platelet count is between 75-100 x10^9/L then the treatment should be delayed until recovery

Hepatic impairment
No prospective study is available in order to establish guidelines for the dose reduction of vinorelbine capsules.

If there is significant hepatic impairment the dose of Vinorelbine soft capsules should be reduced. In patients with massive liver metastases (i.e.> 75% of liver volume replaced by the tumour) it is empirically suggested that a 75% dose be given and the haematological parameters closely monitored.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFTs)

2) Non urgent blood tests- Tests relating to disease response/progression

CONCURRENT MEDICATION

Cytochrome P450 is likely to be mainly involved in the metabolism of vinorelbine, combination with inducers or inhibitors of this isoenzyme may alter its pharmacokinetics. Omeprazole and fluoxetine (norfluoxetine), inhibitors for CYP3A4, were both found to moderately inhibit the metabolism of vinorelbine, although the clinical relevance of this inhibition is not known

ANTIEMETIC POLICY

Moderate emetic risk days 1 and 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Vinorelbine should not be given concomitantly with radiotherapy if the treatment field includes the liver.

REFERENCES

1. NAVELBINE soft capsules http://emc.medicines.org.uk [accessed 25/03/08]

VINORELBINE elderly (oral) (NSCLC)

***Indication:* Palliative treatment of stage III or IV NSCLC or patients not fit enough to tolerate platinum**

NICE guidance www.nice.org.uk. Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.
4 cycles of vinorelbine plus cisplatin are indicated for adjuvant treatment of patients following complete resection of non-small cell lung cancer

DRUG REGIMEN

Cycle 1
Day 1 and 8 **VINORELBINE** 60mg/m^2 orally. (Maximum dose 160 mg/week)

Cycle 2 onwards - dose escalation at the Consultant's discretion if cycle 1 tolerated
Day 1 and 8 **VINORELBINE** 80mg/m^2 (see dose modifications, (Maximum dose 160 mg/week)

NB capsules should be swallowed with food and water without chewing or sucking the capsule at least 30 minutes after antiemetic. Available as 20, 30, 40 and 80mg capsules
NB Based on clinical studies, the oral dose of 80 mg/m^2 was demonstrated to correspond to 30 mg/m^2 of the iv form and 60 mg/m^2 to 25 mg/m^2

Cycle Frequency: every 21 days

DOSE MODIFICATIONS AND DELAYS

Dose escalation from cycle 2 onwards to 80mg/m^2 except in patients for whom the neutrophil count has dropped once below 0.5 x10^9/L OR more than once between 0.5-1.0 x10^9/L during the first cycle doses, in these patients continue at 60mg/m^2

For doses planned to be given at 80mg/m², if the neutrophil count is below 0.5 x10^9/L OR more than once between 0.5-1.0 x10^9/L administration should be delayed until recovery and the dose reduced from 80 to 60mg/m^2 per week during the following cycles.

If the neutrophil count is below 1.5 x10^9/L AND/OR the platelet count is between 75-100 x10^9/L then the treatment should be delayed until recovery

Hepatic impairment
No prospective study is available in order to establish guidelines for the dose reduction of Vinorelbine capsules.

If there is significant hepatic impairment the dose of Vinorelbine soft capsules should be reduced. In patients with massive liver metastases (i.e.> 75% of liver volume replaced by the tumour) it is empirically suggested that a 75% dose be given and the haematological parameters closely monitored.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Liver function tests (LFTs)

2) Non urgent blood tests.- Tests relating to disease response/progression

CONCURRENT MEDICATION

Cytochrome P450 is likely to be mainly involved in the metabolism of vinorelbine, combination with inducers or inhibitors of this isoenzyme may alter its pharmacokinetics. Omeprazole and fluoxetine (norfluoxetine), inhibitors for CYP3A4, were both found to moderately inhibit the metabolism of vinorelbine, although the clinical relevance of this inhibition is not known

ANTIEMETIC POLICY

Moderate emetic risk days 1 and 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Vinorelbine should not be given concomitantly with radiotherapy if the treatment field includes the liver.

REFERENCES

1. NAVELBINE soft capsules http://emc.medicines.org.uk [accessed 25/03/08]

VINORELBINE (oral) CISPLATIN (NSCLC)

Indication: Palliative treatment of unresectable NCSLC.
Adjuvant treatment following complete resection of NSCLC.
Also used as neoadjuvant treatment prior to radical chemoradiotherapy

NICE guidance www.nice.org.uk. Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.
4 cycles of vinorelbine plus cisplatin are indicated for adjuvant treatment of patients following complete resection of non small cell lung cancer

DRUG REGIMEN

Cycle 1
Day 1 Pre-hydration
VINORELBINE 60mg/m^2 orally (Maximum dose 160mg/week)
CISPLATIN 80mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours
Post-hydration
Day 8 **VINORELBINE** 60mg/m^2 orally (Maximum dose 160mg/week)

Cycle 2 onwards - dose escalation at the Consultant's discretion if cycle 1 tolerated
Day 1 Pre-hydration
VINORELBINE 80mg/m^2 orally (Maximum dose 160mg/week)
CISPLATIN 80mg/m^2 infusion in 1000ml sodium chloride 0.9% over 2 hours (daypatient) or 4 hours (inpatient)
Post-hydration
Day 8 **VINORELBINE** 80mg/m^2 orally (Maximum dose 160mg/week)

NB capsules should be swallowed with food and water without chewing or sucking the capsule at least 30 minutes after antiemetic. Available as 20, 30, 40 and 80mg capsules
NB Based on clinical studies, the oral dose of 60mg/m^2 was demonstrated to correspond to 25mg/m^2 of the iv form and 80mg/m^2 to 30mg/m^2, Vinorelbine dose may be increased to 80mg/m^2

Cycle Frequency: Every 21 days
Number of cycles: 2 or 3 if given in neoadjuvant setting, up to 4 in palliative setting, 4 cycles for adjuvant treatment following complete resection (subject to tolerance and response)

DOSE MODIFICATIONS AND DELAYS

Dose escalation from cycle 2 onwards to 80mg/m^2 except in patients for whom the neutrophil count has dropped once below 0.5 x10^9/L OR more than once between 0.5-1.0 x10^9/L during the first cycle doses, in these patients continue at 60mg/m^2

For doses planned to be given at 80mg/m², if the neutrophil count is below 0.5 x10^9/L OR more than once between 0.5-1.0 x10^9/L administration should be delayed until recovery and the dose reduced from 80 to 60mg/m^2 per week during the following cycles.
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If the neutrophil count is below 1.5 x10^9/L AND/OR the platelet count is between 75-100 x10^9/L then the treatment should be delayed until recovery

Hepatic impairment
No prospective study is available in order to establish guidelines for the dose reduction of Vinorelbine capsules.

If there is significant hepatic impairment the dose of Vinorelbine soft capsules should be reduced. In patients with massive liver metastases (i.e.> 75% of liver volume replaced by the tumour) it is empirically suggested that the dose be reduced by 25 % and the haematological parameters closely monitored.

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR < 40ml/min consider carboplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated OR EDTA at the Consultants discretion (Cisplatin).
Liver function tests (LFTs)

2) Non urgent blood tests- Tests relating to disease response/progression

CONCURRENT MEDICATION

Cisplatin - Ensure adequate pre-and post-hydration prescribed as per inpatient schedule at the end of the TVCN regimens. If fluid balance is > 2L positive after 8 hours post hydration OR if patient gains >2kg in weight or urine output <100ml/hour during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.
Vinorelbine- Cytochrome P450 is likely to be mainly involved in the metabolism of vinorelbine, combination with inducers or inhibitors of this isoenzyme may alter its pharmacokinetics. Omeprazole and fluoxetine (norfluoxetine), inhibitors for CYP3A4, were both found to moderately inhibit the metabolism of vinorelbine, although the clinical relevance of this inhibition is not known

ANTIEMETIC POLICY

High emetic risk day 1
Moderate emetic risk day 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Vinorelbine should not be given concomitantly with radiotherapy if the treatment field includes the liver.

REFERENCES

1. Wozniak AJ *et al.* J Clin Oncol 1998; 16: 2459 2465
2. NAVELBINE soft capsules http://emc.medicines.org.uk [accessed 25/03/08]
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

VINORELBINE (oral) CARBOPLATIN (NSCLC)

Indication: Palliative treatment of unresectable NCSLC.
Also used as neoadjuvant treatment prior to radical chemoradiotherapy

NICE guidance www.nice.org.uk. Docetaxel, gemcitabine, paclitaxel and vinorelbine, with a platinum drug, should each be considered as part of first line chemotherapy options for advanced (stage III and IV) NSCLC patients.
4 cycles of vinorelbine plus cisplatin are indicated for adjuvant treatment of patients following complete resection of non-small cell lung cancer

DRUG REGIMEN

Day 1 **VINORELBINE** 60mg/m^2 orally (maximum dose 160mg/week)
CARBOPLATIN AUC5 in 500ml glucose 5% infusion over 60 minutes
Day 8 **VINORELBINE** 60mg/m^2 orally (maximum dose 160mg/week)

NB capsules should be swallowed with food and water without chewing or sucking the capsule at least 30 minutes after antiemetic. Available as 20, 30, 40 and 80mg capsules
NB Based on clinical studies, the oral dose of 60mg/m^2 was demonstrated to correspond to 25mg/m^2 of the iv form and 80mg/m^2 to 30mg/m^2, Vinorelbine dose may be increased to 80mg/m^2

Cycle Frequency: Every 21 days
Number of cycles: 2 or 3 if given in neoadjuvant setting, up to 4 in palliative setting (subject to tolerance and response)

DOSE MODIFICATIONS AND DELAYS

Hepatic impairment
No prospective study is available in order to establish guidelines for the dose reduction of Vinorelbine capsules.

If there is significant hepatic impairment the dose of Vinorelbine soft capsules should be reduced. In patients with massive liver metastases (i.e.> 75% of liver volume replaced by the tumour) it is empirically suggested that the dose be reduced by 25 % and the haematological parameters closely monitored.

Carboplatin:
Discuss if patient has a serum creatinine > 150 micromol/L
If EDTA GFR = or < 20ml/min contraindicated

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

Creatinine clearance (GFR) calculated OR EDTA at the Consultants discretion (Carboplatin).
Liver function tests (LFTs)

2) Non urgent blood tests- Tests relating to disease response/progression

CONCURRENT MEDICATION

Vinorelbine- Cytochrome P450 is likely to be mainly involved in the metabolism of vinorelbine, combination with inducers or inhibitors of this isoenzyme may alter its pharmacokinetics. Omeprazole and fluoxetine (norfluoxetine), inhibitors for CYP3A4, were both found to moderately inhibit the metabolism of vinorelbine, although the clinical relevance of this inhibition is not known

ANTIEMETIC POLICY

High emetic risk day 1
Moderate emetic risk day 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Vinorelbine should not be given concomitantly with radiotherapy if the treatment field includes the liver.

REFERENCES

1. Wozniak AJ *et al.* J Clin Oncol 1998; 16: 2459 2465
2. NAVELBINE soft capsules http://emc.medicines.org.uk [accessed 25/03/08]
3. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network

NHS
Thames Valley

CARBOPLATIN PEMETREXED (Mesothelioma / NSCLC)

Indications: Palliative treatment of non-resectable malignant mesothelioma in patient with an ECOG performance status of 0-1.
First line treatment of Non-small cell lung cancer.

NICE: Pemetrexed is recommended as a possible treatment for malignant pleural mesothelioma in people:
- ***with advanced disease***
- ***whose cancer is not suitable for surgical resection (removal) and***
- ***who have a WHO performance status of 0 or 1***

Pemetrexed is recommended as 1st line treatment of NSCLC adenocarcinoma and large cell undifferentiated carcinoma.

DRUG REGIMEN

Day 1 Pre-medication

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)
PEMETREXED 500mg/m^2 IV infusion in 100ml (Alimta brand use sodium chloride 0.9% but all generic brands use glucose 5%) over 10 minutes
CARBOPLATIN AUC 5 IV infusion in 500ml glucose 5% over 60 minutes
(30 minutes after completing Pemetrexed)

Cycle frequency: ***Every 21 days***
Number of cycles: ***Plan for 3 cycles and repeat cross sectional imaging and full assessment. Maximum 6 cycles depending on tolerance and response.***

DOSE MODIFICATIONS

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
Any Grade 3 or 4 non-haematological toxicities except mucositis	75% of previous dose
Any diarrhoea requiring hospitalisation (irrespective of grade) or Grade 3 or 4 diarrhoea	75% of previous dose
Grade 3 or 4 mucositis	50% of previous dose
Neurotoxicity grade 3 or 4	Discontinue therapy

Treatment with pemetrexed should be discontinued if a patient experiences any haematologic or non-haematologic Grade 3 or 4 toxicity after 2 dose reductions or immediately if Grade 3 or 4 neurotoxicity is observed.
Creatinine clearance (GFR) should be ≥45ml/min (calculated or EDTA) otherwise clinical decision
Liver function tests (LFTs)
Total bilirubin should be ≤1.5 x upper limit of normal.
Alk phos, AST and ALT ≤3 x upper limit of normal. (Alk phos, AST, and ALT ≤5 x normal is acceptable if liver has tumour involvement). Clinical decision

Carboplatin:
Discuss if patient has a serum creatinine > 150 micromol/L
If GFR/ calculated CrCl = or < 20ml/min contraindicated

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent blood tests
Tests relating to disease response/progression

Ideally EDTA GFR should be used (Carboplatin) Creatinine clearance (GFR) calculated, at the Consultants discretion
Liver function tests (LFT)

CONCURRENT MEDICATION

Avoid use of high dose NSAIDs with CrCl > 80ml/min.
Avoid all NSAIDS with CrCl between 45 and 79ml/min for at least 5 days prior to and 2 days after pemetrexed dose.

ANTI-EMETIC POLICY

High emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

REFERENCES

1. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

CISPLATIN PEMETREXED (Mesothelioma / NSCLC)

Indications: Palliative treatment of non-resectable malignant mesothelioma in patient with an ECOG performance status of 0-1.
Pemetrexed is recommended as a possible treatment for locally advanced or metastatic non-small-cell lung cancer (NSCLC) if:
•the cancer is a particular type (adenocarcinoma or large-cell carcinoma) and
•the person has not had any treatment for NSCLC before. NICE TA181

NICE: Pemetrexed is recommended as a possible treatment for malignant pleural mesothelioma in people:
- ***with advanced disease***
- ***whose cancer is not suitable for surgical resection (removal) and***
- ***who have a WHO performance status of 0 or 1***

Pemetrexed is recommended as 1st line treatment of NSCLC adenocarcinoma and large cell undifferentiated carcinoma.

DRUG REGIMEN

Day 1 Pre-medication

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)
Pre-hydration
PEMETREXED 500mg/m^2 IV infusion in 100ml (Alimta brand use sodium chloride 0.9% but all generic brands use glucose 5%) over 10 minutes
CISPLATIN 75mg/m^2 IV infusion in 1000ml sodium chloride 0.9% over 2 hours (30 minutes after completing Pemetrexed)
Post-hydration

Cycle frequency: ***Every 21 days***
Number of cycles: ***Plan for 3 cycles and repeat cross sectional imaging and full assessment. Maximum 6 cycles depending on tolerance and response.***

DOSE MODIFICATIONS

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
Any Grade 3 or 4 non-haematological toxicities except mucositis	75% of previous dose
Any diarrhoea requiring hospitalisation (irrespective of grade) or Grade 3 or 4 diarrhoea	75% of previous dose
Grade 3 or 4 mucositis	50% of previous dose
Neurotoxicity grade 3 or 4	Discontinue therapy

Treatment with pemetrexed should be discontinued if a patient experiences any haematologic or non-haematologic Grade 3 or 4 toxicity after 2 dose reductions or immediately if Grade 3 or 4 neurotoxicity is observed.
Creatinine clearance (GFR) should be ≥45ml/min (calculated or EDTA). Clinical decision
Liver function tests (LFTs)
Total bilirubin should be ≤1.5 x upper limit of normal.
Alk phos, AST and ALT ≤3 x upper limit of normal. (Alk phos, AST, and ALT ≤5 x normal is acceptable if liver has tumour involvement). Clinicial decision

Cisplatin:
GFR >60ml/min give 100% dose
GFR 45-60ml/min give 75% dose
GFR <45ml/min consider carboplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration
2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Ensure adequate pre-and post-hydration prescribed as per inpatient schedule at the end of the TVCN regimens. If fluid balance is > 2L positive after 8 hours post hydration OR if patient gains >2kg in weight or urine output <100ml/hour during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV.
Dexamethasone 4mg bd for 3 days (starting the day before chemotherapy)
Avoid use of high dose NSAIDs with CrCl > 80ml/min. Avoid all NSAIDS with CrCl between 45 and 79ml/min for at least 5 days prior to and 2 days after pemetrexed dose.

ANTI-EMETIC POLICY
High emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.

REFERENCES
1. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

NHS
Thames Valley

PEMETREXED maintenance (NSCLC)

Indication: Locally advanced or metastatic non-small cell lung cancer following treatment with pemetrexed and cisplatin.

NICE: Pemetrexed is recommended as an option for the maintenance treatment of people with locally advanced or metastatic non-small-cell lung cancer other than predominantly squamous cell histology if disease has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel.

For the maintenance treatment of locally advanced or metastatic non-squamous non-small-cell lung cancer in adults when their disease has not progressed immediately after 4 cycles of pemetrexed and cisplatin induction therapy

DRUG REGIMEN

Day 1 Pre-medication

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)
PEMETREXED 500mg/m^2 IV infusion in 100ml (Alimta brand use sodium chloride 0.9% but all generic brands use glucose 5%) over 10 minutes

Cycle frequency: Every 21 days
Number of cycles: Maintenance

DOSE MODIFICATIONS

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
Any Grade 3 or 4 non-haematological toxicities except mucositis	75% of previous dose
Any diarrhoea requiring hospitalisation (irrespective of grade) or Grade 3 or 4 diarrhoea	75% of previous dose
Grade 3 or 4 mucositis	50% of previous dose
Neurotoxicity grade 3 or 4	Discontinue therapy

Treatment with pemetrexed should be discontinued if a patient experiences any haematologic or non-haematologic Grade 3 or 4 toxicity after 2 dose reductions or immediately if Grade 3 or 4 neurotoxicity is observed.

Creatinine clearance (GFR) should be ≥45ml/min (calculated or EDTA). Clinical decision

Liver function tests (LFTs)

Total bilirubin should be ≤1.5 x upper limit of normal.

Alk phos, AST and ALT ≤3 x upper limit of normal. (Alk phos, AST, and ALT ≤5 x normal is acceptable if liver has tumour involvement). Clinicial decision

INVESTIGATIONS

Routine Blood test

1) Blood results required before chemotherapy administration

	Give	*Discuss*
Hb x g/dL	≥10	< 10
Plt x 10^9/L	≥100	< 100
Neutrophils x 10^9/L	≥1.5	< 1.5

2) Non urgent blood tests

Tests relating to disease response/progression

CONCURRENT MEDICATION

Dexamethasone 4mg bd for 3 days (starting the day before chemotherapy)

Avoid use of high dose NSAIDs with CrCl > 80ml/min. Avoid all NSAIDS with CrCl between 45 and 79ml/min for at least 5 days prior to and 2 days after pemetrexed dose.

ANTI-EMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

REFERENCES

1. Daniels, S. and S. Gabriel, *Dosage adjustment for cytotoxics in renal impairment and hepatic impairment*. 2009, The North London Cancer Network.

Pre-hydration and post-hydration regimens

Ensure adequate diuresis is obtained prior to administration and maintained during and after administration.

1. Inpatient

Pre 1L sodium chloride 0.9% + 20mmol KCl + 8mmol $MgSO_4$ infusion over 4 hours
Give cisplatin in 1000ml volume over 4 hours

Post 1L sodium chloride 0.9% + 20mmol KCl + 8mmol $MgSO_4$ infusion over 4 hours
1L sodium chloride 0.9% + 20mmol KCl + 8mmol $MgSO_4$ infusion over 4 hours

NB 1L sodium chloride 0.9% + 20mmol KCl + 8mmol $MgSO_4$ infusion over 6 hours if oral intake is inadequate

2. Day case

Pre 1L sodium chloride 0.9% + 20 mmol KCl + 8mmol $MgSO_4$ infusion over 2 hours
200ml mannitol 10% infusion over 30 minutes (immediately before cisplatin)
Give cisplatin in 1000ml volume over 2 hours

Post 1L sodium chloride 0.9% + 20 mmol KCl + 8mmol $MgSO_4$ infusion over 2 hours

NB Furosemide 40mg may be added if required