Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

ATEZOLIZUMAB-SC-BEVACIZUMAB-CARBOPLATIN (AUC6)-PACLITAXEL

Regimen

- Lung-Atezolizumab-SC-Bevacizumab-Carboplatin (AUC6)-Paclitaxel

Indication

- Atezolizumab in combination with bevacizumab, carboplatin and paclitaxel for the first line treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung cancer with a PD-L1 tumour proportion score of 0-49% and without EGFR and ALK mutations (ATE4).
- Atezolizumab in combination with bevacizumab, carboplatin and paclitaxel for the treatment of adult patients with EGFR or ALK or ROS1 or MET exon 14 or KRAS G12C or RET or BRAF mutation positive locally advanced or metastatic non-squamous non-small cell lung cancer after failure of appropriate targeted therapy (ATE5).
- After completion of the combination of atezolizumab, bevacizumab, carboplatin and paclitaxel and in the absence of disease progression, maintenance treatment with atezolizumab and bevacizumab will continue until loss of clinical benefit or unacceptable toxicity or withdrawal of patient consent or for a maximum treatment duration of 2* years, whichever comes first. 2* years treatment is defined as a maximum of 35 x 3-weekly cycles including the initial 4 induction cycles.

All indications require a Blueteq application, see individual form (ATE4 or ATE5) for specific eligibility criteria. Ensure patient meets Blueteq criteria before consenting patient for treatment.

Toxicity

Drug	Adverse Effect
Atezolizumab	Fatigue, rash, pruritis, pneumonitis, colitis, pancreatitis, diarrhoea, diabetes mellitus, adrenal insufficiency, thyroid disorders, nausea, electrolyte disturbances, hepatitis, myasthenic syndrome, Guillain Barre syndrome
Bevacizumab	Haemorrhage, hypertension, proteinuria, impaired wound healing, gastrointestinal perforations, fistulae, arterial thrombosis
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances
Paclitaxel	Hypersensitivity, hypotension, bradycardia, peripheral neuropathy, myalgia and back pain on administration

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

Monitoring

Drugs

- FBC, LFTs, U&Es and cortisol prior to day each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- Blood pressure and dipstick urinalysis for proteinuria prior to treatment with bevacizumab
- Thyroid function tests prior to starting atezolizumab treatment and then every 6 weeks or when clinically indicated.

Dose Modifications

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

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

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

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Day 1

Neutrophils ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
1 or greater	100%
less than 1	Delay for 7 days. If the counts recover to at least $1x10^9$/L within this time continue with the full dose. If the counts do not recover within 7 days or repeated delays are required then delay until recovery then reduce the dose by 20%
Platelets ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
100 or greater	100%
50-99	Delay for 7 days. If the counts recover to at least $100x10^9$/L within this time then continue with the full dose. If counts do not recover within 7 days or repeated delays are required then delay until recovery then reduce dose by 20%
less than 50	Delay until recovery then reduce dose by 50%

There is little need to adjust the dose of atezolizumab or bevacizumab for haematological toxicity.

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT units	Dose
Atezolizumab	1.5-3xULN	OR	3-5xULN	Delay – see notes below
	Greater than 3xULN	OR	Greater than 3xULN	Discontinue – see notes below
Bevacizumab	N/A		N/A	No information available
Carboplatin	N/A		N/A	No dose adjustment needed
Paclitaxel	less than 21	and	less than 10xULN	175mg/m^2
	21-26			135mg/m^2
	27-51			75mg/m^2
	52-85			50mg/m^2
	greater than 85	or	greater than 10xULN	Contra indicated

For patients with pre-existing mild hepatic impairment no dose adjustment is recommended. Atezolizumab has not been studied in patients with moderate or severe hepatic impairment.

For NCI-CTC grade 2 hepatitis (ALT or AST between 3-5xULN or bilirubin between 1.5-3xULN) that persists for between 5-7 days then withhold the atezolizumab and consider treatment with a corticosteroid. The corticosteroid may be resumed when the event improves to grade 1 or below within 12 weeks and the corticosteroid dose has been reduced to the equivalent of oral prednisolone 10mg per day or less.

For a grade 3 or above hepatitis (ALT or AST greater than 5xULN or bilirubin greater than 3xULN) permanently discontinue atezolizumab

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose
Atezolizumab	N/A	No dose adjustment needed
Bevacizumab	N/A	No information available
Carboplatin*	less than 20	Omit
Paclitaxel	N/A	No dose adjustment needed

* Significant changes in GFR of more than 10% may require dose adjustment.

Other

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

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Atezolizumab

Atezolizumab belongs to the immunotherapy class of cancer treatments. Autoimmune toxicities are most frequently noted and can be life threatening. If autoimmune toxicities occur delaying treatment should be considered while investigations or treatments are organised. Some, but not all, toxicities mandate cessation of treatment. Please seek guidance from relevant site-specific specialist teams or oncologists / haematologists with experience of prescribing these agents. Clinicians should be aware that the current funding approval precludes further treatment after an interruption of 12 weeks or longer; this situation may change.

Refer to the latest version of the European Society of Medical Oncology guidelines; Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[3].

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

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

Atezolizumab should be permanently discontinued for: any NCI-CTC grade 3 or 4 pneumonitis or hepatitis; any other life-threatening NCI-CTC grade 4 reaction (including colitis and renal impairment); any recurrence of a severe or NCI-CTC grade 3 reaction; any persistent NCI-CTC grade 2 or 3 treatment-related adverse reaction that does not recover to grade 1 or resolve within 12 weeks after the last dose.

Immune-related adverse reaction	Severity	Treatment modification
Pneumonitis	Grade 2 pneumonitis	Withhold until symptoms resolve and radiographic abnormalities improve. Consider treatment with oral prednisolone 1-2mg/kg/day or equivalent. Treatment may be resumed if the event improves to grade 0 or grade 1 within 12 weeks, and corticosteroids have been reduced to 10mg or less oral prednisolone equivalent per day.
	Grade 3 or 4 pneumonitis	Permanently discontinue atezolizumab. Consider treatment with corticosteroids.
Colitis	Grade 2 or 3 diarrhoea or symptomatic colitis	Withhold the atezolizumab initially. For a grade 2 diarrhoea or colitis, if the symptoms persist for more than 5 days or recur, start treatment with 1-2mg/kg/day oral prednisolone or equivalent. For a grade 3 diarrhoea or colitis treatment with intravenous corticosteroids should be started, this may be converted to oral treatment as symptoms improve. If the symptoms improve to grade 1 or less taper the corticosteroids over one month Treatment may be resumed if the event improves to grade 0 or grade 1 within 12 weeks, and corticosteroids have been reduced to 10mg or less oral prednisolone equivalent per day
	Grade 4 diarrhoea or colitis	Permanently discontinue atezolizumab. Consider treatment with corticosteroids.
Pancreatitis	Grade 3 or 4 serum amylase or lipase levels increased (more than 2xULN) or grade 2 or 3 pancreatitis	Withhold atezolizumab. Treatment with atezolizumab may be resumed if 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 10mg or less oral prednisolone or equivalent per day
	Grade 4 or any grade of recurrent pancreatitis	Permanently discontinue atezolizumab. Consider treatment with corticosteroids.
Thyroid disorders	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 carbimazole or equivalent and thyroid function is improving
Adrenal insufficiency	Symptomatic	Withhold atezolizumab Treatment may be resumed if the symptoms improve to grade 0 or grade 1 within 12 weeks and corticosteroids have been reduced to the equivalent of 10mg or less of oral prednisone or equivalent per day and patient is stable on replacement therapy
Nephritis	Grade 2	Withhold atezolizumab Start treatment with prednisolone 1-2mg/kg/day or equivalent. Treatment with atezolizumab may be resumed if the symptoms improve to grade 0-1 within 12 weeks and corticosteroids have been reduced to ≤ 10mg prednisolone or equivalent per day.
	Grade 3 or 4	Permanently discontinue atezolizumab
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 prednisolone or equivalent per day and patient is stable on replacement therapy.
	Grade 4	Permanently discontinue atezolizumab.
Type I diabetes mellitus	Grade 3 or 4 hyperglycaemia (fasting glucose more than 250-500mg/dL or 13.9mmol/L)	Withhold atezolizumab Treatment may be resumed if metabolic

		control is achieved on insulin replacement therapy
Myasthenic syndrome / myasthenia gravis, Guillain-Barre syndrome and meningoencephalitis and facial paresis	Facial paresis Grade 1 or 2	Withhold atezolizumab Treatment may be resumed if the event fully resolves. If the event does not fully resolve while withholding atezolizumab, permanently discontinue.
	All Grades Myasthenic syndrome/myasthenia gravis, Guillain Barré syndrome and Meningoencephalitis or Facial paresis Grade 3 or 4	Permanently discontinue atezolizumab
Myositis	Grade 2-3	Withhold atezolizumab
	Grade 4 or recurrent grade 3	Permanently discontinue atezolizumab
Infusion related reactions	Grade 1 or 2	Reduce injection rate or pause injection. Treatment may be resumed when the event has resolved.
	Grade 3 or 4	Permanently discontinue atezolizumab
Rash/severe cutaneous reactions	Grade 3 rash or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	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 10mg or less oral prednisolone or equivalent per day
	Grade 4 rash or confirmed Stevens-Johnson syndrome (SJS) r toxic epidermal necrolysis (TEN)	Permanently discontinue atezolizumab. Consider treatment with corticosteroids

Bevacizumab

Bevacizumab doses should be omitted and not reduced for adverse reactions. If more than two doses are missed due to adverse events treatment should be stopped. It should be noted that the half life of bevacizumab is approximately twenty days. Discontinuation of treatment in response to adverse effects is not expected to influence the short-term clinical evolution of the event, symptomatic treatment is often necessary.

Bevacizumab should be stopped if the individual develops;

- Gastrointestinal perforation
- Arterial thromboembolic events

- NCI-CTC grade 3 and above haemorrhagic events (requiring a blood transfusion or a major non-elective intervention)
- NCI-CTC grade 3 and above congestive heart failure or left ventricular dysfunction.
- NCI-CTC grade 4 fistula

If an NCI-CTC symptomatic grade 4 venous thromboembolic event occurs bevacizumab should be stopped. However, if this is a pulmonary embolism bevacizumab may be re-started once a full recovery has been made and the individual is anti-coagulated with a subcutaneous low molecular weight heparin. An oral anticoagulant must not be used. Hypertension is a common consequence of bevacizumab therapy. For an NCI-CTC grade 1 hypertension no treatment is necessary. NCI-CTC grade 2 hypertension, consider anti-hypertensive therapy. For an NCI-CTC grade 3 and above hypertension that is persistent consider stopping treatment.

Bevacizumab may be continued for an NCI-CTC grade 1 proteinuria or the first occurrence of a grade 2 proteinuria. For the second occurrence of an NCI-CTC grade 2 proteinuria or any NCI-CTC grade 3 proteinuria give the bevacizumab as scheduled. A 24-hour urine collection or UPCR should be conducted at most three days before the next dose. If there is less than 2g protein per 24 hours or a UPCR 0-1 administer the bevacizumab and return to dipstick monitoring. If there is more than 2g protein per 24 hours omit the bevacizumab. Repeat the 24-hour urine collection prior to the next scheduled dose. If this is less than 2g per 24 hours administer the bevacizumab and continue 24-hour urine collection until the protein is 1g per 24 hours or less.

Regimen

Induction - 21 day cycle for 4 cycles

The starting dose of carboplatin AUC6 is used with calculated GFR. AUC5 may be considered with EDTA clearance, seek advice from the appropriate consultant before prescribing. The recommended maximum dose when using a calculated creatinine clearance at AUC6 is 900mg this is set at 890mg in ARIA to comply with national dose bands). If you have an obese patient or an individual with a calculated creatinine clearance above 125mL/min please seek advice from the relevant consultant.

It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

Drug	Dose	Days	Administration
Atezolizumab	1875mg	1	Subcutaneous injection
Bevacizumab	15mg/kg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 90 minutes (see administration information)
Carboplatin	AUC 6 (maximum dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Paclitaxel	200mg/m^2	1	Intravenous infusion in 500ml sodium chloride 0.9% over 180 minutes.

Followed by:

Maintenance – 21 day cycle for a further 31 cycles (35 cycles in total)

Atezolizumab is continued until loss of clinical benefit or unmanageable toxicity

Bevacizumab is continued until disease progression or unacceptable toxicity.

Drug	Dose	Days	Administration
Atezolizumab	1875mg	1	Subcutaneous injection
Bevacizumab	15mg/kg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 90 minutes (see administration information)

Dose Information

- Bevacizumab will be dose banded in accordance with the national dose bands (bevacizumab)
- The recommended maximum dose when using a calculated creatinine clearance at AUC 6 is 900mg (this will be set at 890mg in ARIA to comply with national dose bands). If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.
- It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.
- Carboplatin will be dose banded in accordance with the national dose bands.
- Paclitaxel will be dose banded in accordance with the national dose bands (6mg/ml)
- A lower starting dose of paclitaxel 175mg/m^2 should be used in patients of Asian origin as per the SPC

Administration Information

Extravasation

- Atezolizumab – neutral
- Bevacizumab – neutral
- Carboplatin – irritant
- Paclitaxel - vesicant

Other

- The atezolizumab injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with Atezolizumab SC formulation other medicinal

products for subcutaneous administration should preferably be injected at different sites.

- The first infusion of bevacizumab will be over 90 minutes. If this is well tolerated the second infusion may be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

- Hypersensitivity reactions tend to occur with the first or second infusion of paclitaxel. Paclitaxel infusion should be interrupted for minor symptoms such as flushing or localised rashes. If these resolve promptly (within 5 minutes) the infusion may be restarted at a lower rate with intensive monitoring. Immediately discontinue the infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.

- Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter.

Additional Therapy

- Premedication to reduce of risk of hypersensitivity reaction

  30 minutes before paclitaxel

  - chlorphenamine 10mg intravenous
  - dexamethasone 20mg oral or intravenous
  - H_2 antagonist according to local formulary choice and availability

- Antiemetics

  15-30 minutes prior to chemotherapy (cycles 1-6 only)

  - ondansetron 8mg oral or intravenous

  As take home medication (cycles 1-4 only)

  - dexamethasone 4mg oral twice a day for 3 days
  - metoclopramide 10mg oral three times a day as required

- As required for the treatment of infusion related reactions;

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

- Loperamide 4mg oral initially followed by 2mg after each loose stool when required for the relief of diarrhoea (maximum 16mg/24 hours).

- Gastric protection with a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed

Additional Information

- The use of systemic corticosteroids, before starting treatment with atezolizumab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of the agent. However, systemic corticosteroids can be used after starting atezolizumab to treat immune-related adverse reactions. The use of systemic corticosteroids after starting treatment does not appear to impair the efficacy of atezolizumab.

- Patients must be given an atezolizumab Patient Alert Card.

References

1. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC, MA Socinski, RM Jotte, F Cappuzzo et al. N Engl J Med 2018; 378:2288-2301

2. National Institute for Health and Care Excellence (2019). Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer. NICE technology appraisal guidance 584

3. Haanen J, Carbonnel F, Robert C, Kerr K.M , Peters S, Larkin J, Jordan J on behalf of the ESMO Guidelines Committee. Management of toxicities from immunotherapy. ESMO clinical practice guidelines for diagnosis, treatment and follow up. Ann Oncol 2017; 28 (suppl 4): 119-142.

4. Roche Products Ltd (2023). Tecentriq 1875mg solution for injection Summary of Product Characateristics. Online at https://www.medicines.org.uk/emc/product/15037/smpc last accessed 25/03/2024.

REGIMEN SUMMARY

Atezolizumab-Bevacizumab-Carboplatin (AUC6)-Paclitaxel

Cycle 1, 2, 3, 4

1. Atezolizumab 1875mg subcutaneous injection
   Administration Instructions
   Administer 15 mL of atezolizumab solution for injection subcutaneously into the thigh over approximately 7 minutes. Use of a SC infusion set (e.g. winged/butterfly) is recommended. DO NOT administer the remaining residual hold-up volume in the tubing to the patient.

   Ensure the patient has been given an atezolizumab patient alert card.

2. Bevacizumab 15mg/kg intravenous infusion in 100ml sodium chloride 0.9% over 90 minutes
   Administration Instructions
   The first infusion of bevacizumab will be over 90 minutes. If this is well tolerated the second infusion may be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

3. Chlorphenamine 10mg intravenous

4. Dexamethasone 20mg intravenous

5. H_2 antagonist according to local formulary choice and availability
   Administration Instructions:
   Administer according to local formulary choice and availability one of the following 30 minutes prior to SACT;
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only
   - ranitidine 50mg intravenous once only

   If there is no stock of these products due to national shortages treatment may proceed without the H_2 antagonist provided there is no instruction in the ARIA journal indication the patient **must have** H_2 antagonist treatment.

   All infusion related reactions must be recorded in the ARIA journal and reported to the appropriate consultant. Many Trusts do not administer an H_2 antagonist from cycle three onwards. They have been left in the ARIA protocols so that decisions can be made on an individual Trust and patient basis.

6. Ondansetron 8mg oral or intravenous
   Administration Instructions
   Administer 15-30 minutes before SACT. This may be administered as ondansetron 8mg intravenous if required

7. Warning - Check paclitaxel dose
   Administration Instructions
   A lower starting dose of paclitaxel 175mg/m² should be used in patients of Asian origin as per the SPC

8. Paclitaxel 200mg/m^2 in 500ml sodium chloride 0.9% intravenous infusion over 180 minutes.
   Administration Instructions
   A lower starting dose of paclitaxel 175mg/m² should be used in patients of Asian origin as per the SPC
   Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter

9. Carboplatin AUC 6 (maximum dose) intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   The maximum dose of carboplatin at AUC 6 is 900mg (creatinine clearance 125ml/min). This has been set at 890mg in ARIA to comply with national dose bands

10. Chlorphenamine 10mg intravenous injection when required for infusion related reactions

11. Hydrocortisone 100mg intravenous injection when required for infusion related reactions

12. Paracetamol 1000mg oral when required for infusion related reactions
    Administration Instructions
    Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines

13. Dexamethasone 4mg oral twice a day for 3 days starting on day 2 of the cycle

14. Metoclopramide 10mg oral three times a day for three days then 10mg three times a day when required for nausea
    Administration Instructions
    When required for the relief of nausea. Please supply five days or an original pack as appropriate

15. Loperamide as directed (cycle 1 only)
    Administration Instructions
    Take 4mg after the first loose stool then 2mg after each subsequent loose stool to a maximum dose of 16mg / 24 hours

Cycle 5-35

16. Atezolizumab 1875mg subcutaneous injection
    Administration Instructions
    Administer 15 mL of atezolizumab solution for injection subcutaneously into the thigh over approximately 7 minutes. Use of a SC infusion set (e.g. winged/butterfly) is recommended. DO NOT administer the remaining residual hold-up volume in the tubing to the patient.
    Ensure the patient has been given an atezolizumab patient alert card.

17. Bevacizumab 15mg/kg intravenous infusion in 100ml sodium chloride 0.9% over 90 minutes
    Administration Instructions
    The first infusion of bevacizumab will be over 90 minutes. If this is well tolerated the second infusion may be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

18. Chlorphenamine 10mg intravenous injection when required for infusion related reactions

19. Hydrocortisone 100mg intravenous injection when required for infusion related reactions

20. Paracetamol 1000mg oral when required for infusion related reactions
    Administration Instructions
    Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.0	March 2024	None	Eleanor Taylor Oncology Pharmacist	Judith Cave Consultant Medical Oncologist

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

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

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.