Chemotherapy Protocol

BREAST CANCER

PEMBROLIZUMAB WITH CARBOPLATIN/PACLITAXEL AND EC NEOADJUVANT BREAST CANCER FOLLOWED BY ADJUVANT PEMBROLIZUMAB

Regimen

- Breast-Pembrolizumab with Carboplatin/Paclitaxel and EC followed by Pembrolizumab Monotherapy

Indication

- Pembrolizumab in combination with chemotherapy as neoadjuvant treatment and then continued as adjuvant monotherapy after definitive surgery for patients with previously untreated locally advanced or early-stage triple negative breast cancer at high risk of recurrence.

- Performance status 0, 1

This indication requires a Blueteq application, see individual form (PEMB21) for specific eligibility criteria. Ensure patient meets Blueteq criteria before consenting patient for treatment.

Toxicity

Drug	Adverse Effect
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances
Cyclophosphamide	Dysuria, haemorrhagic cystitis, taste disturbances
Epirubicin	Cardiotoxicity, urinary discolouration (red)
Paclitaxel	Hypersensitivity, hypotension, bradycardia, peripheral neuropathy, myalgia and back pain on administration
Pembrolizumab	Pneumonitis, nephritis, colitis, thyroid disorders, hypophysitis, infusion related reactions, hepatitis

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

Monitoring

Drugs

Neoadjuvant phase (cycles 1-8)

- FBC, U&Es, LFTs, Magnesium prior to days 1, 8 and 15 for cycles 1 and 2; on day 1 only from cycle 3 onwards at clinicians' discretion.
- Cortisol, TFTs and blood glucose prior to day 1
- EDTA or calculated creatinine clearance prior to day 1 of each cycle
- ECG/ECHO prior to starting cycle 5 if clinically indicated.

Adjuvant phase (cycles 9-17)

- FBC, U&Es, LFTs, TFTs, cortisol and blood glucose every 6 weeks.

Dose Modifications

The dose modifications listed are for haematological, hepatic, 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 or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L)

Neoadjuvant phase

Carboplatin/paclitaxel (cycles 1-4)

Neutrophils ($x10^9$/L)		**Platelets** ($x\ 10^9$/L)	**Carboplatin dose**	**Paclitaxel dose**
≥ 1.0	and	≥ 100	100%	100%
< 1.0	or	< 100	Delay 1 week (or until recovery) then reduce dose by 1 x AUC	Delay 1 week (or until recovery) *
< 1.0	and	< 100	Delay 1 week (or until recovery) then reduce dose by 1 x AUC	Delay 1 week (or until recovery) then reduce dose to 70mg/m^2)*

***Omit paclitaxel if occurring on **day 8 or 15**

In the case of febrile neutropenia (neutrophils < 0.5 × 10^9/L and fever > 38.5°C requiring IV antibiotics) reduce paclitaxel to 60mg/m^2 and carboplatin by 1 x AUC for all subsequent doses.

Epirubicin/cyclophosphamide (cycles 5-8)

Neutrophils ($x10^9$/L)		**Platelets** ($x\ 10^9$/L)	**Epirubicin dose**	**Cyclophosphamide dose**
< 1.0	and/or	< 100	Delay 1 week or until recovery	Delay 1 week or until recovery
<0.5 for more than 1 week or febrile neutropenia despite G-CSF			Consider 20% dose reduction for future cycles	Consider 20% dose reduction for future cycles

Adjuvant Phase

Pembrolizumab (cycles 9-17)

Discuss with the consultant if:
Neutrophils < $1.0x10^9$/L
Platelets < 75×10^9/L

Hepatic Impairment

Drug	Bilirubin (µmol/L)	Dose (% of original)	AST/ALT	Dose (% of original)
Carboplatin	No dose adjustment needed			
Cyclophosphamide	Dose reduction may not be necessary			
Epirubicin	24-51	50	2-4 x ULN	50
	52-85	25	>4 x ULN	25
	>85	Contraindicated		
Paclitaxel	51 or greater	Not recommended	N/A	
Pembrolizumab	No dose reduction is necessary in those with mild hepatic impairment (see below for management of transaminitis)			

Renal Impairment

Drug	Creatinine Clearance (mL/min)	Dose (% of original dose)
Carboplatin*	less than 20	Omit
Cyclophosphamide	More than 20	100%
	10-20	75%
	10 or less	50%
Epirubicin	No data on use in severe renal impairment. Consider dose reduction if CrCl <10mL/min	
Paclitaxel	N/A	No dose adjustment needed
Pembrolizumab	No dose adjustment is required for mild to moderate renal impairment (see below for management of nephritis)	

*The GFR should be recalculated, or re-measured, due to:

- renal toxicity (serum creatinine greater than 1.5xULN)
- serum creatinine changes of 10% or greater compared to baseline, or last creatinine value used to calculate carboplatin dose (whichever is most recent)

Pembrolizumab

Hepatic Impairment

For a hepatitis associated with an AST / ALT of 3-5xULN and / or a total bilirubin of 1.5-3xULN then withhold treatment and administer corticosteroids. Upon improvement to NCI-CTC grade 1 hepatic injury begin to taper the corticosteroid over a period of one month. The

pembrolizumab may be re-started when the liver function remains at NCI-CTC grade 1 following corticosteroid taper.

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

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

Renal Impairment

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

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

Other

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

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

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

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

Endocrine

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

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

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

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

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

Eye

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

Gastrointestinal

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

mucosal inflammation, with or without ulcerations and lymphocytic and neutrophilic infiltration.

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

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

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

Lung

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

Should a second episode of pneumonitis occur then discontinue pembrolizumab.

For NCI-CTC grade 3 or 4 events discontinue pembrolizumab and consider pulmonary function tests and seek advice from a lung specialist. A bronchoscopy with biopsy and / Or BAL should be considered. Treatment involves corticosteroid therapy such as intravenous methylprednisolone 125mg. When symptoms improve to NCI-CTC grade 1 or less, a high dose oral steroid such as prednisone 1 to 2 mg/kg once per day can be considered. A reducing schedule should be considered over a period of at least four weeks. taper should be started and continued over no less than 4 weeks. If intravenous corticosteroids followed by high dose oral corticosteroids do not reduce initial symptoms within 48 to 72 hours, treat with infliximab at 5 mg/kg once every 2 weeks. Discontinue infliximab upon symptom relief and initiate a prolonged steroid taper over 45 to 60 days. If symptoms worsen during steroid reduction, initiate a retapering of steroids starting at a higher dose followed by a more prolonged taper and administer infliximab.

Skin

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

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

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

Regimen

Neoadjuvant phase

Paclitaxel/carboplatin and pembrolizumab – 21 day cycle (cycles 1-4)

The starting dose of carboplatin AUC5 is used with calculated GFR. AUC4 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 AUC5 is 750mg (creatinine clearance 125mL/min). This is not a dose included in the national dose banding table. The maximum dose has been set at 790mg in ARIA. Please check if this dose is appropriate. 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
Pembrolizumab	200mg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes with a 0.2 micron filter
Paclitaxel	80mg/m^2	1, 8, 15	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes.
Carboplatin	AUC 5 (max dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes

Followed by

Epirubicin/cyclophosphamide and pembrolizumab – 21 day cycle (cycles 5-8)

Cycle 5 commences 21 days after the 4th dose of carboplatin (ie usually 7 days after week 12 of paclitaxel)

Drug	Dose	Days	Administration
Pembrolizumab	200mg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes with a 0.2 micron filter
Epirubicin	90mg/m2	1	Intravenous bolus
Cyclophosphamide	600mg/m2	1	Intravenous bolus

Adjuvant Phase

Pembrolizumab monotherapy – 21 day cycle (cycles 9-17)

Drug	Dose	Days	Administration
Pembrolizumab	200mg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes with a 0.2 micron filter

Dose Information

- Carboplatin will be dose banded in accordance with the national dose bands (10mg/mL)
- The recommended maximum dose of carboplatin when using a calculated creatinine clearance at AUC 5 is 750mg. This dose is NOT included in the national dose banding table. The maximum dose therefore has been set at 790mg in ARIA. Please check if this dose is appropriate.
- Paclitaxel will be dose banded in accordance with the national dose bands (6mg/mL)
- Epirubicin will be dose banded in accordance with the national dose bands (2mg/mL)
- Cyclophosphamide will be dose banded in accordance with the national dose bands (20mg/mL)
- Pembrolizumab is dosed at a flat dose of 200mg administered every 3 weeks in the neoadjuvant and adjuvant phases of treatment.

Administration Information

Extravasation

- Carboplatin – irritant
- Paclitaxel – vesicant
- Epirubicin – vesicant
- Cyclophosphamide – neutral
- Pembrolizumab – neutral

Other

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

- Antiemetics

  Cycles 1-4

  30minutes prior to chemotherapy

  - netupitant and palonosetron 300mg/0.5mg (Akynzeo) oral (day 1)
  - metoclopramide 10mg oral or intravenous (day 8 & 15)

  Cycles 5-8

  30 minutes prior to chemotherapy
  - netupitant and palonosetron 300mg/0.5mg (Akynzeo) oral (day 1)
  - dexamethasone 8mg oral (day 1)
  - olanzepine 10mg oral (day 1)

  As take home medication (day 1 only)
  - olanzepine 10mg oral at night for 3 days starting on day 2 (dose can be reduced to 5mg if sedation is a concern)

- Growth factor as per local formulary choice;

  Cycles 1-4
  - filgrastim or bioequivalent 30million units once a day on days 3-5, 10-12 and 17-19 of the cycle subcutaneous
  - lenograstim or bioequivalent 33.6million units once a days 3-5, 10-12 and 17-19 of the cycle subcutaneous

  Cycles 5-8
  - filgrastim or bioequivalent 30million units once a day for 5 days starting on day 3 of the cycle subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 5 days starting on day 3 of the cycle subcutaneous
  - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once a day on day 2 of the cycle subcutaneous

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

- Mouthwashes if required for prevention of mucositis.

Additional Information

- Ensure the patient has been given a pembrolizumab Patient Alert Card

References

1. National Institute for Health and Care Excellence (2022). Pembrolizumab for neoadjuvant and adjuvant treatment of triple-negative early or locally advanced breast cancer. NICE technology appraisal guidance 851.

2. The Clatterbridge Cancer Centre NHS Foundation Trust (2022). Systemic Anti Cancer Therapy Protocol Pembrolizumab with Carboplatin/Paclitaxel and EC Neoadjuvant Breast Cancer Regimen followed by Adjuvant Pembrolizumab. Online at https://www.clatterbridgecc.nhs.uk/application/files/2617/1517/9660/Pembrolizumab_with_Carboplatin_Paclitaxel_and_EC_Neoadjuvant_Breast_Cancer_Regimen_followed_by_Adjuvant_Pembrolizumab.pdf Last accessed 15/07/2024

3. Somerset, Wiltshire, Avon and Gloucestershire Cancer Alliance (2022). Carboplatin & Weekly Paclitaxel / EC (Epirubicin &Cyclophosphamide) with Pembrolizumab (Breast) Protocol. Online at https://www.swagcanceralliance.nhs.uk/wp-content/uploads/2022/10/Pembro-Carbo-Wkly-Taxol-EC-v1.pdf last accessed 18/3/2024

4. Merck Sharp and Dohme (UK) Ltd (2024). KEYTRUDA 25 mg/mL concentrate for solution for infusion Summary of Product Characteristics. Online at https://www.medicines.org.uk/emc/product/2498 last accessed 18/03/024.

5. New England Journal of Medicine 2020;382:810-21

6. European Society for Medical Oncology (2023). 2023 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting. Online at https://www.esmoopen.com/action/showPdf?pii=S2059-7029%2823%2901436-9 Last accessed 15/07/2024

REGIMEN SUMMARY

Neoadjuvant Phase

Paclitaxel/carboplatin and pembrolizumab – 21 day cycle (cycles 1-4)

Cycles 1,2,3 and 4, Day 1

1. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
   Administration Instructions
   Administer via a 0.2 to 5 µm in-line low protein binding filter.

2. Netupitant and palonosetron 300mg/0.5mg oral
   Administration Instructions
   To be administered 60 minutes before chemotherapy

3. Chlorphenamine 10mg intravenous
   Administration instructions:
   To be administered 30 minutes before paclitaxel

4. Dexamethasone 10mg intravenous
   Administration instructions:
   To be administered 30 minutes before paclitaxel

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 indicating 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. Paclitaxel 80mg/m^2 in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes.
   Administration Instructions
   Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22micron filter

7. Warning - Carboplatin Maximum Dose
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at

790mg in ARIA. Please check this dose is appropriate for your patient.

8. Carboplatin AUC 5 (max dose) intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient

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

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

11. 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 Cycles 1,2,3 and 4, day 1

12. Growth Factor as directed
    Administration instructions:
    Growth factor as per local formulary choice:
    - filgrastim or bioequivalent 30million units once a day on days 3-5, 10-12, 17-19 of the cycle subcutaneous
    - lenograstim or bioequivalent 33.6million units once a day on days 3-5, 10-12, 17-19 of the cycle subcutaneous

Cycles 1,2,3 and 4, Days 8 & 15

13. Chlorphenamine 10mg intravenous
    Administration instructions:
    To be administered 30 minutes before paclitaxel

14. Dexamethasone 10mg intravenous
    Administration instructions:
    To be administered 30 minutes before paclitaxel

15. H_2 antagonist according to local formulary choice and availability
    Administration Instructions:
    Administer according to local formulary choice and availability one of the following;
    - ranitidine 50mg intravenous once only
    - famotidine 20mg oral once only
    - Nizatidine 150mg oral once only
    - Ranitidine 150mg oral once only

16. Metoclopramide 10mg oral or intravenous

17. Paclitaxel 80mg/m^2 in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes.
    Administration Instructions
    Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter

Epirubicin/cyclophosphamide and pembrolizumab - 21 day cycle (cycles 5-8)

Cycles 5,6,7 and 8 (day1)

18. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
    Administration Instructions
    Administer via a 0.2 to 5 µm in-line low protein binding filter.

19. Netupitant and palonosetron 300mg/0.5mg oral
    Administration Instructions

To be administered 60 minutes before chemotherapy

20. Olanzapine 10mg oral
    Administration Instructions
    To be administered 60 minutes before chemotherapy

21. Dexamethasone 8mg oral or intravenous
    Administration Instructions
    Administer 15-30 minutes prior to chemotherapy
    This may be given as dexamethasone IV stat if required

22. Epirubicin 90mg/m² intravenous bolus over 10 minutes

23. Cyclophosphamide 600mg/m² intravenous bolus over 10 minutes

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

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

26. 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
Cycles 5,6,7 and 8, day 1

27. Olanzapine 10mg once a day at night for 3 days.
    Administration Instructions
    Starting on the day after chemotherapy.

28. Growth Factors according to local formulary choice.
    Administration instructions:
    - filgrastim or bioequivalent 30million units once a day subcutaneous for 5 days starting on day 3 of the cycle.
    - lenograstim or bioequivalent 33.6million units once a day subcutaneous for 5 days starting on day 3 of the cycle
    - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once a day subcutaneous on day 2 of the cycle for 1 day

Adjuvant Phase

Pembrolizumab monotherapy

Cycles 9-17, day 1

29. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
    Administration Instructions
    Administer via a 0.2 to 5 µm in-line low protein binding filter.

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

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

32. 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	September 2024	New Protocol	Eleanor Taylor Oncology Pharmacist	Dr Sanjay Raj 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.