Chemotherapy Protocol

UROTHELIAL CANCER

Enfortumab vedotin-Pembrolizumab (EV-P)

Regimen

- Urothelial – Enfortumab vedotin - Pembrolizumab

Indication

- First-line treatment of adult patients with unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy.

This indication requires a Blueteq application, see individual form (ENF1) for specific eligibility criteria. Ensure patient meets Blueteq criteria before consenting patient for treatment.

Toxicity

Drug	Common	Uncommon	Rare
Enfortumab Vedotin	Alopecia, anaemia, hypothyroidism, hyperglycaemia, peripheral sensory neuropathy, decreased appetite, dysgeusia, dry eye(s), diarrhoea, nausea, vomiting, pruritis, rash, fatigue	Thrombocytopenia, pneumonitis/ILD, Infusion related reaction, peripheral motor neuropathy	Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), neurotoxicity
Pembrolizumab	Respiratory tract infections, hyperglycaemia, dyspnoea, cough, rash, pruritis, arthralgia, fatigue, hypothyroidism, deranged LFTs/electrolytes	Arthritis, stomatitis, pneumonitis, colitis, hyperthyroidism, infusion related reactions, hepatitis, dry skin, hypertension, hypoglycaemia	Nephritis, myocarditis, diabetes, uveitis, adrenal insufficiency, hypophysitis, hypopituitarism, SJS, TEN

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

Monitoring

Regimen

- **Prior to Cycle 1 day 1:**
  FBC, LFTs, U&Es, LDH, thyroid function, glucose, calcium, cortisol and HbA1c.
  Consider ECG, Troponin, NT Pro-BNP and Echocardiogram (in high-risk patients i.e. known CV disease, previous cardiotoxic therapy).

- **Prior to day 1 in subsequent cycles:**
  FBC, U&Es and LFTs, glucose, thyroid function tests and cortisol

- **Prior to day 8**
  FBC, U&Es and LFTs and glucose

Dose Modifications

Dose level	**Dose**
Starting dose	1.25mg/kg (max dose 120mg)*
First dose reduction	1.0mg/kg (max dose 100mg)
Second dose reduction	0.75mg/kg (max dose 75mg)
Third dose reduction	0.5mg/kg (max dose 50mg)

*Max licensed dose is 125mg, 120mg will be given due to National Dose Banding)

The dose modifications listed are for haematological, liver, 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.

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

If neutrophils are < $1.0x10^9$/L or platelets < 75 x 10^9/L withhold enfortumab vedotin until recovery. Restart at the same dose or dose reduction as per table below:

Toxicity			**Action**
Neutrophils 0.5-0.99 x 10^9/L	*or*	Platelets 25 – 99 x 10^9/L	Consider restarting at same dose or at a one level dose reduction – consultant decision
Neutrophils < 0.5 x 10^9/L	*or*	Platelets < 25 x 10^9/L	Restart at one level dose reduction

There is little need to adjust the dose of pembrolizumab for haematological toxicity.

Hepatic Impairment

Enfortumab vedotin

No dose adjustment is necessary in patients with mild hepatic impairment [total bilirubin of 1 to 1.5 × upper limit of normal (ULN) and AST any, or total bilirubin ≤ ULN and AST > ULN].

Enfortumab vedotin has only been evaluated in a limited number of patients with moderate and severe hepatic impairment. Hepatic impairment is expected to increase the systemic exposure to MMAE (the cytotoxic part of the antibody drug conjugate); therefore, patients should be closely monitored for potential adverse events. No specific dose recommendations are available.

Pembrolizumab

No dose adjustment is needed for patients with mild hepatic impairment. Pembrolizumab has not been studied in moderate or severe hepatic impairment but no need for dose adjustment is expected – discuss with consultant. See below for management of hepatitis emergent on treatment.

Renal Impairment

	Mild/moderate	**Severe**	**End stage renal disease**
Enfortumab vedotin	No dose adjustment is required where CrCl ≥ 15mL/min		Not evaluated
Pembrolizumab	No dose adjustment is required where CrCl ≥30mL/min	Not studied but no need for dose adjustment expected (discuss with consultant if CrCl < 30mL/min)	
*See below for management of nephritis emergent on pembrolizumab treatment.			

Other toxicities

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.

Enfortumab vedotin

Enfortumab vedotin is an antibody drug conjugate (ADC) targeting Nectin-4 (an adhesion protein located on the surface of urothelial cancer cells). It is made up of a fully human IgG1-kappa antibody conjugated to the microtubule-disrupting agent MMAE (vedotin).

Skin reactions

Skin reactions are common during treatment and patients should be monitored throughout treatment. Median time to onset of severe skin reactions was 1.7 months (range 0.1-17.2 months). Antihistamine and topical corticosteroids can be considered for mild to moderate skin reactions.

For suspected toxic epidermal necrolysis or Stevens-Johnson syndrome withhold treatment and urgently refer to dermatology.

Pneumonitis/Interstitial Lung Disease

Patients should be monitored for symptoms such as hypoxia, cough and dyspnoea or signs such as interstitial infiltrates on radiologic exams. Administer corticosteroids for ≥ Grade 2 events e.g. prednisolone 1-2mg/kg/day.

Hyperglycaemia

Hyperglycaemia occurred more frequently in patients with pre-existing hyperglycaemia or a high body mass index (≥30 kg/m2). Patients with baseline HbA1c ≥8% were excluded from clinical studies.

Blood glucose levels should be monitored prior to dosing and periodically throughout the course of treatment as clinically indicated in patients with or at risk for diabetes mellitus or hyperglycaemia.

Ocular disorders

Ocular disorders, predominantly dry eye, have occurred in patients treated with enfortumab vedotin. Patients should be monitored for any ocular symptoms. Consider dose interruption or dose reduction of Enfortumab vedotin for symptomatic ocular disorders.

Consider artificial tears for prophylaxis of dry eye and refer for ophthalmologic evaluation if ocular symptoms do not resolve or worsen.

Toxicity	Definition	Dose modification
Skin reactions	Grade 1-2	Withhold until grade < 1. Restart at same dose or consider one level dose reduction.
	Grade 2 with fever or grade 3	Withhold until grade < 1. Restart at same dose or consider one level dose reduction.
	Suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) or bullous lesion	Immediately withhold treatment and refer to dermatology
	Confirmed SJS or TEN; grade 4 or recurrent grade 3	Permanently discontinue enfortumab vedotin
Hyperglycaemia	Blood glucose > 13.9mmol/L	Withhold enfortumab vedotin until blood glucose has improved to ≤13.9 mmol/L. Resume treatment at the same dose level.
Pneumonitis/ Interstitial lung disease	Grade 2	Withhold until grade ≤ 1. Restart at same dose or consider one level dose reduction.
	Grade ≥ 3	Permanently discontinue enfortumab vedotin
Peripheral neuropathy	Grade 2	Withhold until grade ≤ 1 For first occurrence, resume treatment at same dose level. For recurrent toxicity, reduce dose by one level
	Grade ≥ 3	Permanently discontinue enfortumab vedotin
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.		

Pembrolizumab

Autoimmune toxicities are most frequently noted and can be life threatening. Please seek guidance from relevant site-specific specialist teams or oncologists / haematologists with experience of prescribing these agents.

Immune-related adverse reactions, which can be severe or life-threatening, may involve the gastrointestinal, liver, skin, nervous, endocrine, or other organ systems. If autoimmune toxicities occur, delaying treatment should be considered while investigations or treatments are organised.

Some, but not all, toxicities mandate cessation of treatment. 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.

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 constitute 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 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 grade 3 or above ocular symptoms and consider treatment with systemic corticosteroids. When symptoms improve to 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.

Grade 1 diarrhoea or suspected mild colitis may continue pembrolizumab. Symptomatic treatment and close monitoring are advised.

For grade 2-3 colitis withhold the pembrolizumab and administer corticosteroids. Upon improvement to grade 1 begin to taper the corticosteroid over a period of one month. Restart pembrolizumab when the colitis remains at grade 1 following corticosteroid taper.

The pembrolizumab should be permanently discontinued when the colitis does not improve to at least 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 grade 3 or above reaction.

Lung

Interstitial lung disease including pneumonitis and acute interstitial pneumonitis are associated with pembrolizumab.

For grade 1 events (asymptomatic with radiographic findings only) continue pembrolizumab 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 grade 2 events withhold 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 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 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 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 grade 1 or less, a high dose oral steroid such as prednisone 1 to 2 mg/kg once per day can be considered. A reducing schedule should be considered over a period of at least four weeks. If intravenous corticosteroids followed by high dose oral corticosteroids do not

reduce initial symptoms within 48 to 72 hours, 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 re-tapering 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 have been reported. Pembrolizumab can also be associated with pruritus, rash, (generalized and maculo-papular) and vitiligo. All attempts should be made to rule out other causes such as metastatic disease, infection or allergic dermatitis.

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

For 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 grade 1 or less then steroid taper should be started and continued over no less than 4 weeks.

Other

Uveitis, arthritis, myositis, myocarditis, pancreatitis, Guillain-Barré syndrome, myasthenic syndrome, haemolytic anaemia, sarcoidosis, encephalitis, myelitis, vasculitis, cholangitis sclerosing, gastritis, cystitis noninfective, hypoparathyroidism and pericarditis have been reported in clinical studies. Based on the severity and type of the adverse reaction, pembrolizumab should be withheld for Grade 2 or Grade 3 events and corticosteroids administered.

Pembrolizumab may be restarted within 12 weeks if the adverse reaction recovers to Grade ≤ 1 and corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day.

Pembrolizumab must be permanently discontinued for any Grade 3 immune-mediated adverse reaction that recurs and for any Grade 4 immune-mediated adverse reaction.

For Grades 3 or 4 myocarditis, encephalitis or Guillain-Barré syndrome, pembrolizumab should be permanently discontinued.

Toxicity	Definition	Dose modification
Colitis	Grade 1	Continue and closely monitor
	Grade 2-3	Withhold until symptoms resolve to ≤ grade 1
	Grade 4 or recurrent grade 3	Permanently discontinue pembrolizumab
Pneumonitis	Grade 1	Continue and closely monitor
	Grade 2	Withhold until symptoms resolve to ≤ grade 1
	Grade 3-4 or recurrent grade 2	Permanently discontinue pembrolizumab
Nephritis	Grade 2 (creatinine 1.5-3 x ULN) or Grade 3 (creatinine > 3 x ULN)	Withold until symptoms resolve to ≤ grade 1
	Grade 4 (creatinine > 6 x ULN)	Permanently discontinue
Endocrine	Grade 2 adrenal insufficiency and hypophysitis	Withhold treatment until controlled by hormone replacement
	Grade 3 or 4 adrenal insufficiency or symptomatic hypophysitis	Withhold until symptoms resolve to ≤ grade 1
	Type 1 diabetes with grade > 3 hyperglycaemia (glucose >13.9 mmol/L) or ketoacidosis	Withhold until ≤ grade 2 May consider recommencing after corticosteroid taper or discontinue.

	Hyperthyroidism ≥ grade 3	Withhold until ≤ grade 2 May consider recommencing after corticosteroid taper or discontinue
	Hypothyroidism	Continue and manage with replacement therapy
Hepatitis	Grade 2: AST/ALT 3-5 x ULN or Bilirubin > 1.5-3 x ULN	Withhold until resolves to ≤ grade 1
	Grade 3: AST/ALT 5-20 x ULN or Bilirubin 3-10 x ULN	May consider recommencing after corticosteroid taper or discontinue treatment – consultant decision
	Grade 4: AST/ALT > 20 x ULN or Bilirubin > 10 x ULN	Permanently discontinue pembrolizumab
	If liver metastasis and baseline AST/ALT 3-5 x ULN and AST/ALT increases ≥ 50% from baseline for ≥ 1 week	Permanently discontinue pembrolizumab
Skin	Grade 3 rash	Withhold until resolves to ≤ grade 1
	Grade 4 rash or Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Permanently discontinue pembrolizumab
Cardiac	Grade 2 myocarditis	Withhold until resolves to ≤ grade 1
	Grade 3 or 4 myocarditis	Permanently discontinue pembrolizumab
Neurological	Grade 2 motor or sensory neuropathy	Withhold until resolves to ≤ grade 1
	Grade 3 or 4 motor or sensory neuropathy	Permanently discontinue pembrolizumab
	Grade 3 or 4 encephalitis	Permanently discontinue pembrolizumab
	Grade 3 or 4 Guillain-Barré syndrome	Permanently discontinue pembrolizumab
Infusion-related reactions	Grade 3-4	Permanently discontinue pembrolizumab
Any other toxicity	Grade 3 (first occurrence)	Withhold until resolves to ≤ grade 1
	Grade 4 or recurrent Grade 3	Permanently discontinue pembrolizumab
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.		

Pembrolizumab should be permanently discontinued if:

- Corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks
- Treatment-related toxicity does not resolve to Grade 0-1 within 12 weeks after last dose

Regimen

21-day cycle

Drug	Dose	Days	Route
Enfortumab Vedotin	1.25mg/kg (maximum 120mg)	1, 8	Intravenous infusion in 100mL sodium chloride 0.9 % over 30 minutes via a 0.2 micron in-line filter
Pembrolizumab	200mg**	1	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes via a 0.2 micron in-line filter

*Enfortumab maximum dose set to 120mg due to National Dose Banding.
**Pembrolizumab may also be administered as 400mg very 6 weeks, i.e. on alternate 21-day enfortumab vedotin cycles.

Number of cycles

Enfortumab vedotin: Until disease progression or unacceptable toxicity.
Pembrolizumab: Up to a maximum of 35 x 3 weekly cycles (or equivalent if given 6 weekly).
If either drug is stopped due to toxicity the remaining agent can continue as a single agent within the above parameters, in terms of overall duration.

Administration Information

- Enfortumab vedotin is administered as an intravenous infusion in 50-100mL sodium chloride 0.9% over 30 minutes. Enfortumab vedotin should be administered via an infusion set with a 0.2micron filter.
- Pembrolizumab should be administered **after** enfortumab vedotin when they are both administered on the same day. Pembrolizumab should be administered in 100mL sodium chloride 0.9% over 30 minutes via an infusion set with an in-line sterile, non-pyrogenic, low protein binding filter (pore size 0.2 – 5.0µm).
- Observe a 30-minute interval between the 2 infusions for at least cycle 1, day 1. If well-tolerated this interval can be reduced to 15 minutes on subsequent infusions.

Extravasation

- Enfortumab vedotin – irritant with vesicant-like properties
- Pembrolizumab – neutral

Additional Therapy

- Low emetogenic regimen, no routine antiemetics are required

- As required for the treatment of infusion related reactions;
  - chlorphenamine 10mg intravenous
  - hydrocortisone 100mg intravenous
  - paracetamol 1000mg oral

- 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

- Artificial tears for prophylaxis of dry eye(s)

- Hydrocortisone 1% cream, emollient and chlorphenamine may be required if skin toxicity develops

Additional Information

- Females of reproductive potential should be advised to use effective contraception during treatment and for at least 6 months after stopping treatment. Men being treated with enfortumab vedotin are advised not to father a child during treatment and for at least 4 months following the last dose.

Drug interactions – for full details consult the product literature/interactions sources

- **Strong CYP3A4 and P-gp inhibitors (e.g., ketoconazole)** may increase the AUC of unconjugated MMAE (the cytotoxic component of enfortumab vedotin) to a minor extent. Closely monitor patients for signs of toxicity when enfortumab vedotin is given concomitantly with dual P-gp and strong CYP3A4 inhibitors.
- **Strong CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenobarbital, phenytoin, St John's wort)** may decrease exposure to unconjugated MMAE.
- **Corticosteroids:** use of systemic corticosteroids, before starting treatment with pembrolizumab 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 pembrolizumab to treat immune-related adverse reactions. The use of systemic corticosteroids after starting treatment does not appear to impair the efficacy of pembrolizumab

References

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REGIMEN SUMMARY

Enfortumab vedotin – Pembrolizumab (EV-P)

Cycle One, Day One

1. Enfortumab vedotin 1.25mg/kg (max. dose 120mg) intravenous infusion in 100mL sodium chloride 0.9% over 30 minutes
   Administration Instructions
   Enfortumab vedotin should be administered via an infusion set with a 0.2-micron filter

2. Pembrolizumab 200mg intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
   Administration Instructions
   Pembrolizumab should be administered using a low protein binding filter

3. Chlorphenamine 10mg intravenous when required for the treatment of infusion related reactions

4. Hydrocortisone sodium succinate 100mg intravenous when required for the treatment of infusion related reactions

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

Cycle One, Day Eight

6. Enfortumab vedotin 1.25mg/kg (max. dose 120mg) intravenous infusion in 100mL sodium chloride 0.9% over 30 minutes
   Administration Instructions
   Enfortumab vedotin should be administered via an infusion set with a 0.2-micron filter

7. Chlorphenamine 10mg intravenous when required for the treatment of infusion related reactions

8. Hydrocortisone sodium succinate 100mg intravenous when required for the treatment of infusion related reactions

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

Take Home Medicines – Day 1

10. Metoclopramide 10mg oral three times a day when required for nausea
    Administration Instructions
    Supply an original pack on cycle one only

11. Artificial Tears one drop into each eye when required for the relief of dry eyes
    Administration Instructions
    Supply an original pack

12. Zerobase cream topically four times a day when required for dry skin Administration Instructions
    To be used as a general moisturiser and a soap substitute for the prevention/relief of dry skin. Supply 500g on cycle one only

13. Chlorphenamine 4mg oral three times a day when required for the relief of itchy skin
    Administration Instructions
    Supply an original pack on cycle one day 1 only

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.0	March 2026	New Protocol	Eleanor Taylor Oncology Pharmacist	Prof. Simon Crabb Consultant Oncologist

This systemic anticancer therapy (SACT) 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
Isle of Wight NHS Trust
Portsmouth University 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.