Chemotherapy Protocol

GERM CELL

Amb TICE (Part 2): Carboplatin – Etoposide phosphate

Ambulatory Regimen
This regimen is for AMBULATORY CARE pathway use only use only and will only be available to prescribe at units which carry out autograft transplantation.

This treatment regimen consists of two parts: 2 cycles of TI (Paclitaxel and Ifosfamide) followed by 3 cycles of
CE (Carboplatin and Etoposide) with PBSC autologous transplant.

Regimen

- Germ Cell – Amb TICE (part 2): Carboplatin and Etoposide phosphate

Indication

- Conditioning for autologous peripheral blood stem cell transplant (PBSCT) / bone marrow transplant in individuals with relapsed and refractory metastatic germ cell tumours.

Toxicity

Drug	Adverse Effect
Carboplatin	Neuropathy, hypersensitivity, nephrotoxicity, ototoxicity
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia

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

Monitoring

Drugs

- EDTA or calculated creatinine clearance before the 1st cycle.
- FBC, LFTs and U&Es prior to each cycle

Dose Modifications

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

In principle all dose reductions 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. The following is a general guide only.

Haematology

Treatment will be given regardless of blood results.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. Irradiated blood products must be used.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (%of original dose)
Carboplatin	No adjustment necessary			
Etoposide (as etoposide phosphate)	26-51	or	60-180	50
	more than 51	or	more than 180	clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carboplatin	Less than 50	Do not use
	Changes in the GFR of more than 10% between cycles may require dose adjustment	
Etoposide (as etoposide phosphate)	more than 50	100
	15-50	75
	less than 15	50

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.

Regimen

The starting dose of carboplatin AUC8 is maxed at 1200mg; unless GFR is measured using EDTA and patient is over 18 in which case dose can exceed 1200mg after consultant review (ref NCI/CTEP letter Ivy et al 2010)

Etoposide phosphate (Etopophos) must be used for this protocol as solutions of conventional etoposide would exceed the maximum concentration of 0.4 mg/mL and may precipitate.

NOTE: 1 mg of etoposide = 1.136 mg etopophos (etoposide phosphate). Doses in this protocol are expressed as etoposide whereas all administration details in this protocol refer to Etoposide phosphate.

Consider a dose reduction in poor performance patients.

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.

21 day cycle for 3 cycles

Drug	Dose	Days	Administration
Carboplatin	AUC8	-5, -4, -3	Intravenous infusion in 500ml glucose 5% over 60 minutes
Etoposide (as etoposide phosphate)	400mg/m^2	-5, -4, -3	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Dose Information

- Carboplatin will be dose banded according to the national dose band (10mg/ml)
- Etoposide dose will be rounded to the nearest 100mg (up if halfway)

Administration Information

Extravasation

- Carboplatin – irritant
- Etoposide - irritant

Additional Therapy

This regimen is to be administered in the ambulatory setting. Please ensure all supportive and take-home medicines are prescribed on the in-patient chart or general electronic prescribing system if patient requires admission. Please refer to the transplant schedule for each individual patient.

This therapy may lead to the development of tumour lysis syndrome at the start of therapy. Patients should be assessed and for those patients deemed high risk allopurinol should be prescribed. This should begin the day before chemotherapy treatment and continue for as long as a significant chemo-sensitive tumour bulk remains.

- **Antiemetics**
  - Starting 15-30 minutes prior to chemotherapy: Aprepitant 125mg once only orally on the day -5 then 80mg once a day for the subsequent two days
  - dexamethasone 2mg twice a day for 3 days oral or intravenous starting on day -5 of the cycle

- metoclopramide 10mg three times a day for 10 days oral or intravenous starting on day -5 of the cycle
- ondansetron 8mg twice a day oral or intravenous

- **Anti-infectives**
  - aciclovir 400mg oral twice a day
  - ciprofloxacin 250mg oral twice a day from day +1 (stop when neutrophils are greater than 1)
  - fluconazole 100mg once a day oral (stop when neutrophils are greater than 1 unless the patient remains on corticosteroids)
  - nystatin suspension 1ml four times a day oral (stop when neutrophils are greater than 1 unless the patient remains on corticosteroids)

- **Thromboprophylaxis,** to be started on Day +5, unless patient has been deemed high risk. To be continued until platelets are less than $50x10^9$/L, or as directed by the consultant, according to VTE risk assessment and local formulary choices:
  - dalteparin 5000units once a day subcutaneous injection
  - enoxaparin 40mg once a day subcutaneous injection
  - heparin 5000units twice a day subcutaneous injection
  - Anti-embolism (TED) stockings

- **Growth factors** such as filgrastim biosimilar 30million units (300mcg) once a day subcutaneous from day +5 (stop when neutrophils are greater than $1x10^9$/L for at least 24 hours, or greater than 3 on any occasion). This will not be supplied pre-admission, and to be prescribed on admission day +5.

- **Hormone replacement**
  In menstruating women consider norethisterone 5mg three times a day oral to prevent menstruation. This may be stopped when the platelets are more than $50x10^9$/L.

- **Mouthcare** for the prophylaxis or treatment of mucositis in accordance with local or national guidelines.

- **Gastric protection** with a proton pump inhibitor or a H2 antagonist according to local formulary choice:
  - esomeprazole 20mg once a day oral
  - omeprazole 20mg once a day oral
  - lansoprazole 15mg once a day oral
  - pantoprazole 20mg once a day oral
  - rabeprazole 20mg once a day oral
  - cimetidine 400mg twice a day oral
  - famotidine 20mg once a day oral
  - nizatidine 150mg twice a day oral

- **Hydration**
  Encourage 2L oral fluids daily. If ambulatory patients are unable to maintain this (e.g. due to nausea), they should be admitted for intravenous hydration.

Additional Information

- Irradiated blood products must be used
- Autologous stem cells/ bone marrow will be infused on day 0

References

1. Mummaneni, V., Kaul, S., Igwemezie, L.N. *et al.* Bioequivalence assessment of etoposide phosphate and etoposide using pharmacodynamic and traditional pharmacokinetic parameters. *Journal of Pharmacokinetics and Biopharmaceutics* **24**, 313–325 (1996). https://doi.org/10.1007/BF02353515

2. Neon Healthcare Ltd. Etopophos 100mg Powder for Solution for Injection Summary of Product Characteristics. Electronic Medicines Compendium [Internet]. 2024. Available from: Etopophos 100 mg Powder for Solution for Injection - Summary of Product Characteristics (SmPC) - (emc) | 10514

3. Cancer Institute NSW – eviQ. Chemotherapy protocol: Autologous conditioning germ cell tumour TICE (cARBOplatin and etoposide) (part 2). [Internet]. 2011. Last reviewed 2022. Available from: 1178-Autologous conditioning germ cell tumour TICE (cARBOplatin and etoposide) (part 2) | eviQ

REGIMEN SUMMARY

Germ Cell – Amb TICE (part 2): Carboplatin and Etoposide phosphate

Day -5

1. Aprepitant 125mg capsule oral

2. Dexamethasone 2mg oral or intravenous

3. Ondansetron 8mg oral or intravenous

4. Metoclopramide 10mg oral or intravenous

5. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

6. Carboplatin AUC8 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   This recommended maximum dose is 1200mg based on a creatinine clearance of 125ml/min.

7. Etoposide 400mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
   Administration Instructions
   Etoposide phosphate (Etopophos) must be used for this protocol as solutions of conventional etoposide would exceed the maximum concentration of 0.4 mg/mL and may precipitate.

8. Sodium chloride 0.9% 1000ml intravenous infusion over 4 hours

Take Home Medicines

9. Dexamethasone 2mg once a day in the afternoon for 3 days starting on day -5

10. Ondansetron 8mg once a day in the evening for 3 days starting on day -5, then take 8mg twice a day for 3 days.

11. Metoclopramide 10mg twice a day in the afternoon and evening for 3 days starting on day -5, then take 10mg three times a day for 3 days.
    Administration instructions –Please supply 28 tablets or an original pack as appropriate

12. Aciclovir 400mg three times a day for 28 days
    Administration Instructions Please supply 28 days or an original pack if appropriate.

13. Ciprofloxacin 250mg twice a day starting on day +1
    Administration Instructions: Stop when neutrophils are greater than 1.0. Please supply 14 days with no stop date

14. Fluconazole 100mg oral once a day
    Administration instructions – stop when neutrophils are greater than 1.0 unless the patient remains on corticosteroids. Please supply 14 days with no stop date.

15. Nystatin 1ml four times a day
    Administration instructions – stop when neutrophils are greater than 1.0 unless the patient remains on corticosteroids. Please supply 1 x OP

16. Gastric Protection

Administration Instructions The choice of gastric protection is dependent on local formulary choice and may include;
- esomeprazole 20mg once a day oral
- omeprazole 20mg once a day oral
- lansoprazole 15mg once a day oral
- pantoprazole 20mg once a day oral
- rabeprazole 20mg once a day oral
- cimetidine 400mg twice a day oral
- famotidine 20mg once a day oral
- nizatidine 150mg twice a day oral

Please supply 28 days or the nearest original pack size.

17. Sodium Chloride 0.9% oral rinse 10mL four times a day

Administration instructions – pharmacy please supply 50 x 10mL pods

18. Thromboprophylaxis according to local formulary choice

To start on admission, on Day +5, unless the patient is deemed high risk. Continued until platelets are less than $50x10^9$/L, or as directed by the consultant, according to local formulary choices:

- dalteparin 5000units once a day subcutaneous injection
- enoxaparin 40mg once a day subcutaneous injection
- heparin 5000units twice a day subcutaneous injection

Please supply 28 days or nearest original pack size.

19. Warning – Ensure take home medicines are supplied

Day -4, day -3

20. Aprepitant 80mg once a day oral

21. Dexamethasone 2mg oral or intravenous

22. Ondansetron 8mg oral or intravenous

23. Metoclopramide 10mg oral or intravenous

24. Sodium chloride 0.9% 500ml intravenous infusion over 60 minutes

25. Carboplatin AUC8 intravenous infusion in 500ml glucose 5% over 60 minutes

Administration Instructions

This recommended maximum dose is 1200mg based on a creatinine clearance of 125ml/min.

26. Etoposide 400mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Administration Instructions

Etoposide phosphate (Etopophos) must be used for this protocol as solutions of conventional etoposide would exceed the maximum concentration of 0.4 mg/mL and may precipitate.

27. Sodium chloride 0.9% 1000ml intravenous infusion over 4 hours

Day -2, Day -1

Rest day

Day 0

28. Chlorphenamine 10mg Intravenous bolus
    Administration instructions – to be given pre stem cell infusion

29. Paracetamol 1000mg Tablet Oral
    Administration instructions – to be given pre stem cell infusion

30. Stem Cell Return – see separate chart

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	09/12/2025	None	Alexandre Guedes Pharmacist	Robert Lown Consultant

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;

University Hospital Southampton 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.