Chemotherapy Protocol

BRAIN TUMOURS

CARBOPLATIN (AUC5)-ETOPOSIDE

Regimen

- Brain – Carboplatin (AUC5)-Etoposide

Indication

- Third line treatment of glioblastoma multiforme
- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Carboplatin	Neuropathy, hypersensitivity
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

Regimen

- 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

Prior to prescribing on day one of cycle one the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Consider blood transfusion if patient symptomatic of anaemia or haemoglobin of less than 8g/dL(80g/L)

Subsequently if the neutrophils are less than $1x10^9$/L then, in the first instance delay treatment for seven days. If counts recover at this point continue at the initial dose. If counts remain low continue with treatment using 80% of the last dose. If the myelosuppression re-curs despite this dose reduction stop treatment.

If the platelets are 50-$99x10^9$/L then, in the first instance delay treatment for seven days. If the counts recover at this point continue at the initial dose. If the counts still fall within this range continue using of the last dose. If the platelet level falls below $50x10^9$/L reduce the dose by 50%.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (%of original dose)
Carboplatin	No adjustment necessary			
Etoposide	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 20	Do not use
	Changes in the GFR of more than 10% between cycles may require dose adjustment	
Etoposide	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 AUC 5 is used with calculated GFR. AUC 4 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.

28 day cycle for 6 cycles

Drug	Dose	Days	Administration
Carboplatin	AUC 5 (max dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Etoposide	100mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Dose Information

- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC 5 is 750mg. This will be set as 790mg in ARIA to comply with national dose bands.
- Etoposide (intravenous) will be dose banded in accordance with the national dose bands (20mg/ml)

Extravasation

- Carboplatin – irritant
- Etoposide - irritant

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy;

  - ondansetron 8mg oral or intravenous
  - dexamethasone 8mg oral or intravenous

  As take home medication;

  - dexamethasone 4mg twice a day oral for 3 days
  - metoclopramide 10mg three times a day oral
  - ondansetron 8mg twice a day for 3 days

These patients are often on long-term dexamethasone, and their daily dose of dexamethasone can be taken into account when prescribing and administering anti-emetic dexamethasone

- for patients on a daily dose totalling 8mg or more of dexamethasone, no extra dexamethasone needs to be prescribed as an anti-emetic

- for patients on a total daily dose of less than 8mg dexamethasone, the daily dose needs to be increased to 8mg daily on days 1 to 4 of the cycle only.

- on days 2, 3 and 4, the dose may either be taken as 4mg twice a day, or the total dose may be taken once daily in the morning, whichever the patient is used to, or prefers.

- 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

- Prophylactic antibiotics can be considered if required

References
1. Tonder M, Weller M, Eisele G et al. Carboplatin and etoposide in heavily pre-treated patients with progressive high grade glioma. Chemotherapy 2014; 60 (5-6): 375-378.

REGIMEN SUMMARY

Carboplatin (AUC5)-Etoposide

Day One

1.Warning – Check dexamethasone dose

Administration Instructions.

These patients are often on long-term dexamethasone, and their daily dose of dexamethasone can be taken into account when prescribing and administering anti-emetic dexamethasone;

-for patients on a daily dose totalling 8mg or more of dexamethasone, no extra dexamethasone needs to be prescribed as an anti-emetic

- for patients on a total daily dose of less than 8mg dexamethasone, the daily dose needs to be increased to 8mg daily on days 1 to 4 of the cycle only.

- on days 2, 3 and 4, the dose may either be taken as 4mg twice or the total dose may be taken once daily in the morning, whichever the patient is used to, or prefers.

2.Dexamethasone 8mg oral or intravenous

Administration Instructions

This may be given as 8mg intravenous stat if required

These patients are often on long-term dexamethasone, and their daily dose of dexamethasone can be taken into account when prescribing and administering anti-emetic dexamethasone;

-for patients on a daily dose totalling 8mg or more of dexamethasone, no extra dexamethasone needs to be prescribed as an anti-emetic

- for patients on a total daily dose of less than 8mg dexamethasone, the daily dose needs to be increased to 8mg daily on days 1 to 4 of the cycle only.

- on days 2, 3 and 4, the dose may either be taken as 4mg twice or the total dose may be taken once daily in the morning, whichever the patient is used to, or prefers.

3. Ondansetron 8mg oral or intravenous bolus

Administration Instructions

This may be given as ondansetron 8mg intravenous if required

4. 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.

5. Carboplatin AUC 5 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

6. Etoposide 100mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Take Home Medicines

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

Administration Instructions
Take 4mg twice a day for 3 days starting on day 2 of the cycle.

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-for patients on a daily dose totalling 8mg or more of dexamethasone, no extra dexamethasone needs to be prescribed as an anti-emetic

- for patients on a total daily dose of less than 8mg dexamethasone, the daily dose needs to be increased to 8mg daily on days 1 to 4 of the cycle only.

- on days 2, 3 and 4, the dose may either be taken as 4mg twice or the total dose may be taken once daily in the morning, whichever the patient is used to, or prefers.

8.Metoclopramide 10mg three times a day when required oral

Administration Instructions
Please supply 28x10mg tablets or nearest equivalent pack size

9. Ondansetron 8mg twice a day oral for 3 days starting on the evening of first day of chemotherapy

Administration Instructions
Take 8mg twice a day for three days starting on the evening of day one of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Aug 2022	Carboplatin national dose bands changed Coding removed Administration Instructions added to summary Warning added to summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	Jan 2019	None	Dr Deborah Wright Pharmacist	Dr Jeng Ching Consultant Clinical 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 Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Trust

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