Chemotherapy Protocol

Central Nervous System

LOMUSTINE

Regimen

- CNS – Lomustine

Indication

- Adjuvant treatment for grade III gliomas including anaplastic astrocytoma, oligodendrogliomas and oligoastrocytomas.
- First line treatment for grade IV tumours not eligible for concurrent chemoradiation regimen.
- Recurrent high grade gliomas.
- Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Lomustine	Myelosuppression, pulmonary fibrosis

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

Monitoring

Drugs

- FBC, LFT's, U&E's and glucose prior to day one of each cycle
- Clinical examination including neurological assessment, whole brain imaging prior to starting treatment.

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

Prior to starting treatment 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 has a haemoglobin of less than 8g/dL.

If the platelets and / or neutrophils are greater than $100x10^9$/L and $1.5x10^9$/L respectively then continue with therapy. If the platelets were between 80 to $100x10^9$/L and the neutrophils between 1–$1.5x10^9$/L then continue with treatment at 80% of the last dose. If the platelets were less than 80 or neutrophils less than $1x10^9$/L delay treatment for seven days. If counts recover at this point continue with treatment using 60% of the last dose. If a second delay is necessary consider stopping therapy. The haematological toxicity of lomustine may be cumulative, leading to successively lower white cell and platelet counts with successive doses of the drug.

Hepatic Impairment

Drug	Bilirubin (µmol/L)	AST/ALT	Dose
Lomustine	more than 25	more than 5xULN	omit or dose reduce

Renal Impairment

Creatinine Clearance (ml/min)	Lomustine Dose
more than 60	100%
45 – 60	75%
30 - 45	50%
less than 30	Not recommended

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 2 toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. For toxicity that is NCI-CTC grade 3 or above discontinue treatment.

Regimen

42 day cycle for 6 cycles or until tumour progression (6 cycles will be set in Aria)

Drug	Dose	Days	Administration
Lomustine	100mg/m^2 once a day	1	Oral

Dose

- Lomustine is available as 40mg capsules. The dose will be rounded to the nearest 40mg (up if halfway)
- In some instances the dose may be increased to 110mg/m^2. Please seek consultant advice

Administration Information

- Lomustine capsules must be swallowed whole with a glass of water and must not be opened or chewed.

Additional Therapy

Antiemetics

- 15-30 minutes prior to chemotherapy
    - dexamethasone 8mg oral (omit if patient is already taking dexamethasone)
    - ondansetron 8mg oral
    - metoclopramide 10mg three times a day when required for the relief of nausea
- Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday
- 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.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to oral lomustine.

Coding

- Procurement – X70.2
- Delivery – X73.1

References
1.Medical Research Council Brain Tumor Working Party: Randomized trial of procarbazine, lomustine, and vincristine in the adjuvant treatment of high-grade astrocytoma: A Medical Research Council trial. J Clin Oncol (2001); 19: 509-518
2.Levin VA, Silver P, Hannigan J et al. Superiority of post-radiotherapy adjuvant chemotherapy with CCNU, procarbazine, and vincristine (PCV) over BCNU for anaplastic gliomas: NCOG 6G61 final report. Int J Radiat Oncol Biol Phys (1990); 18 (2): 321-

REGIMEN SUMMARY

LOMUSTINE

Cycle 1 – Day 1

Take Home Medicines

1. Dexamethasone 8mg oral
   Administration Instructions
   Omit this dose if the patient is already taking dexamethasone.

2. Ondansetron 8mg 15-30 minutes prior to lomustine oral
   An additional dose may be taken 12 hours later if required for the treatment of nausea and vomiting. This contains sufficient supply for six cycles.
   Please supply an original pack (10 tablets) or nearest equivalent to cover 6 cycles of treatment.

3. Lomustine 100mg/m^2 once a day for one day oral
   Administration Instructions
   Swallow whole with a full glass of water. Do not open or chew.

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

5. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
   Administration Instructions
   Please supply for 42 days

Cycle 2, 3, 4, 5, 6 - Day 1

Take Home Medicines

1. Dexamethasone 8mg oral
   Administration Instructions
   Omit this dose if the patient is already taking dexamethasone.

2. Lomustine 100mg/m^2 once a day for one day oral
   Administration Instructions
   Swallow whole with a full glass of water. Do not open or chew

3. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
   Administration Instructions
   Please supply for 42 days

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Oct 2015	None	Dr Deborah Wright Pharmacist	Dr Omar Al Salihi 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 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, it remains the responsibility of the prescriber to ensure the correct drugs and doses are prescribed for patients.