

Chemotherapy Protocol
Central Nervous System
LOMUSTINE-PROCARBAZINE

[Regimen](#)

- CNS – Lomustine-Procarbazine

[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
Procarbazine	Rash, loss of appetite, flu like symptoms

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 $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

Consider blood transfusion or erythropoietin according to NICE technology appraisal if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

If the platelets and / or neutrophils are less than $100 \times 10^9/L$ and $1.5 \times 10^9/L$ respectively then delay therapy until counts recover to these levels. If more than one delay is necessary in treatment due to neutropenia or thrombocytopenia, reduce procarbazine duration from 10 days to 7 days. 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 ($\mu\text{mol/L}$)	AST/ALT	Dose
Lomustine	more than 25	and more than 180	omit or dose reduce
Procarbazine	more than 50	normal	50%
	more than 85	or more than 180	omit

Renal Impairment

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

For procarbazine, if the serum creatinine is more than $177 \mu\text{mol/L}$, give 50% dose. Procarbazine is not recommended with severe renal failure (creatinine clearance less than 10mL/min).

[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.

If the patient develops a rash, they should stop procarbazine immediately. Procarbazine should then be omitted from future cycles.

[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
Procarbazine	100mg/m ² once a day	1-10 inclusive	Oral

[Dose](#)

- Lomustine is available as 40mg capsules. The dose will be rounded to the nearest 40mg (up if halfway)
- Procarbazine is available as 50mg capsules. Doses will be rounded to the nearest 25mg. Different alternate day dosing may be required to ensure the total dose is administered.

[Administration Information](#)

- Lomustine and procarbazine 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
 - domperidone 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 H₂ 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 and procarbazine
- Procarbazine is a weak MAO inhibitor and therefore certain foodstuffs should be avoided. These foods include mature cheeses (including processed cheese, but cottage cheese and cream cheese are safe), yeast or meat extracts (Marmite, Oxo, Bovril), broad bean pods, pickled herring, salami sausage, flavoured textured vegetable protein, over-ripe fruit, alcoholic drinks (especially heavy red wines such as Chianti), non- alcoholic beers, lagers and wines, other foods that are not fresh, particularly if they have been fermented, pickled, smoked, “hung” (game), or “matured”, miso soup and large amounts of soy sauce.

Coding

- Procurement – X70.2
- Delivery – X 72.3

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: NCOG6G61 final report. *Int J Radiat Oncol Biol Phys* (1990); 18 (2): 321-4.

REGIMEN SUMMARY

LOMUSTINE-PROCARBAZINE

Day 1

Take Home Medicines

1. Lomustine 100mg/m² once a day for one day oral
Administration Instructions
Swallow whole with a full glass of water. Do not open or chew
2. Procarbazine 100mg/m² once a day for ten days oral
Administration Instructions
Swallow whole with a full glass of water. Do not open or chew. Do not drink alcohol.
Procarbazine is available as 50mg capsules. To facilitate alternate day dosing in Aria the dose will be rounded to the nearest 25mg (up if halfway).
If the calculated dose is 125mg please dispense 150mg alternating with 100mg daily.
If the calculated dose is 175mg please dispense 200mg alternating with 150mg daily.
If the calculated dose is 225mg please dispense 250mg alternating with 200mg daily.
3. Dexamethasone 8mg oral 15-30 minutes prior to lomustine
Administration Instructions
Omit this dose if the patient is already taking dexamethasone.
4. Domperidone 10mg three times a day when required oral
5. Ondansetron 8mg oral 15-30 minutes prior to lomustine
6. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
Administration Instructions
Please supply 42 days

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Oct 2015	Dose rounding to 25mg added to procarbazine. Additional instructions added to summary in administration instructions	Dr Deborah Wright Pharmacist	Dr Omar Al Salihi Consultant Clinical Oncologist
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.