Lomustine (CNS)

Indication
Palliative therapy for advanced/recurrent glioma.

ICD-10 codes
Codes prefixed with C71

Regimen details

Day	Drug	Dose	Route
1	Lomustine	100mg/m^2	PO

Cycle frequency
42 days

Number of cycles
6 cycles

Administration
Lomustine is available as 40mg capsules. Lomustine capsules should be swallowed whole with water.

Pre-medication
5HT3-antagonist before lomustine on day 1 and BD on day 2.

Emetogenicity
This regimen has high emetogenic potential.

Additional supportive medication
Mouthwash as per local policy
Laxatives as required.

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U+E (including creatinine)	7 days
LFT	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9 /L
Platelet count	≥ 100 x 10^9 /L
Creatinine clearance	≥ 60 mL/min
Bilirubin	≤ 1.5 x ULN
ALT/AST	< 3 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9 /L or platelets < 100 x 10^9 /L - delay one week or until recovery and consider 75% dose of lomustine.

In the case of febrile neutropenia (neutrophils < 0.5 × 10^9 /L and fever > 38.5°C requiring IV antibiotics) delay one week or until FBC recovers and consider reducing lomustine to 75% dose.

If platelets < 50 x 10^9 /L - delay one week or until recovery and consider reducing lomustine to 60% dose.

- **Renal impairment**

Creatinine Clearance CrCl (mL/min)	Lomustine Dose
>60	100%
45-60	75%
30-44	50%
<30	Discontinue

- **Hepatic impairment**

AST/ALT (xULN)		Bilirubin (xULN)	Lomustine Dose
<3	and	≤ 1.5	100%
3-5	and/or	1.5 - 5	50%
>5	or	>5	Omit

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Pneumonitis / pulmonary fibrosis
Thromboembolism
Nephrotoxicity
Hypersensitivity and allergic reactions
Secondary malignancy
Myocardial infarction
SIADH
Teratogenicity
Infertility

- **Frequently occurring side effects**

Nausea or vomiting
Fatigue, flu-like symptoms
Anorexia, weight loss
Constipation, diarrhoea
Myelosuppression
Stomatitis/mucositis

- **Other side effects**

Rash
Alopecia
CNS depression
Insomnia
Hepatotoxicity
Deranged LFTs

Significant drug interactions – for full details consult product literature/ reference texts

Lomustine is a major CYP2D6 substrate and a weak CYP2D6 and CYP3A4 inhibitor.

Theophylline: concomitant use may potentiate bone marrow toxicity

Cimetidine: concomitant use may potentiate bone marrow toxicity.

Phenytoin and fosphenytoin: close monitoring and/or alternative agents are recommended if co-prescribed with this regimen. Phenytoin serum levels may be decreased, possibly as a result of decreased absorption and/or increased metabolism.

Barbiturates: Phenobarbital can lead to a reduced anti-tumour effect of lomustine due to induction of hepatic enzymes and increased elimination.

Additional comments

Haematological toxicity may be cumulative.

Lomustine can cause pulmonary problems after high, lifetime cumulative doses (>1,100mg/m2). Onset of symptoms may occur months/years after treatment discontinued.

References

- Krens S D, Lassche, Jansman GFGA, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20:e201-08. Supplementary appendix
- Summary of Product Characteristics Lomustine (medac). Accessed 3 August 2023 via www.medicines.org.uk
- Lomustine Monograph. Accessed December 2022 via http://www.bccancer.bc.ca
- Wick, W. et al. Lomustine and Bevacizumab in Progressive Glioblastoma. N Engl J Med 2017; 377:1954-1963.

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