Lomustine

Indication
Palliative therapy for advanced/recurrent glioma.

ICD-10 codes
Codes prefixed with C71.

Regimen details
Lomustine 160mg orally **once only**.

Cycle frequency
Every 6 weeks (42 days)

Number of cycles
6 cycles or until disease progression
Further treatment is associated with increased risk of pulmonary toxicity and renal toxicity (see notes below)
Discontinue lomustine for progressive disease or intolerable side effects

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

Pre-medication
$5HT_3$-antagonist before BD for 2 days (take first dose before lomustine).

Emetogenicity
This regimen has high emetogenic potential on days 1 and 2 due to lomustine.

Additional supportive medication
Metoclopramide 10mg po tds prn

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT – including AST	14 days

Investigations –pre subsequent cycles
FBC, U+E (including creatinine), LFT (including AST)

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
AST	< 1.5 x ULN

Dose modifications

- **Haematological toxicity**

Neutrophils		Platelets	Lomustine dose
> 1.5 x 10^9/L	and	> 150 x 10^9/L	Give 100%
1.0 – 1.5 x 10^9/L	and	75 – 150 x 10^9/L	Give 80%. Discuss with consultant
< 1.0 x 10^9/L	and	< 75 x 10^9/L	Delay therapy for 1-2 weeks and resume at 60% of the original lomustine dose Discuss with consultant

- **Renal Impairment**

CrCl (mL/min)	**Lomustine dose**
>60	100%
45-60	75%
30-44	50%
<30	Discontinue

Renal failure – Cumulative Lomustine dose

Renal failure has been reported in single cases after prolonged treatment with lomustine reaching a high cumulative total dose. Therefore it is recommended not to exceed a maximum cumulative lomustine dose of 1000mg/m2

- **Hepatic impairment**

Bilirubin(x ULN)	**AST / ALT** (x ULN)	**Lomustine dose**
≤ 1.5	≤ 1.5	100%
1.5 - 3	1.5-3	100%
>3 - 5	>3-5	Consider dose reduction
>5	>5	Consider dose reduction

Lack of available information. Transient elevation of liver enzymes have occasionally been observed. Assess liver function periodically and if severe hepatic impairment, consider dose reduction. Discuss with consultant

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
Bowel perforation
Pancreatitis
Myocardial infarction
SIADH
Teratogenicity
Infertility

- **Frequently occurring side effects**

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

- **Other side effects**

Rash, pigmentation, photosensitivity
CNS depression, nightmares, hallucinations, insomnia

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

Coumarin-derived anticoagulants such as warfarin: patients established on warfarin should either be changed to low molecular weight heparin or have weekly monitoring of INR. Patients who are initiated on anti-coagulation should remain on low molecular weight heparin until completion of the course of chemotherapy.
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/m^2). Onset of symptoms may occur months/years after treatment discontinued.

References

- http://www.swscn.org.uk/guidance-protocols/cancer-protocols/ accessed 10 May 2020
- Summary of Product Characteristics Lomustine (medac). Accessed 9 March 2019 via www.medicines.org.uk

THIS PROTOCOL HAS BEEN DIRECTED BY DR LAM, DESIGNATED LEAD CLINICIAN FOR NEURO-ONCOLOGY

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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