

PCV - Procarbazine, Lomustine and Vincristine (CNS)

Indication

Palliative therapy for advanced/recurrent glioma.
Adjuvant treatment for patients with co-deleted anaplastic tumours.

ICD-10 codes

Codes prefixed with C71.

Regimen details

Day	Drug	Dose	Route
1	Vincristine	1.5mg/m ² (max. 2mg)	IV infusion
1	Lomustine	100mg/m ²	PO
1 to 10	Procarbazine	100mg/m ²	PO

Cycle frequency

Every 6 weeks (42 days)

Number of cycles

6 cycles

Administration

Vincristine is administered as an intravenous infusion in 50mL sodium chloride 0.9% over 10 minutes, as per national guidance. The nurse should remain with patient throughout infusion.

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

Procarbazine is available as 50mg capsules. Procarbazine should be swallowed whole with water.

Pre-medication

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

Emetogenicity

This regimen has moderate emetogenic potential (with high emetogenic potential on days 1 and 2 due to lomustine).

Additional supportive medication

Nil

Extravasation

Vincristine is a vesicant (Group 5).

Investigations – pre first cycle

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

Investigations –pre subsequent cycles

Investigation	Validity period (or as per local policy)
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	$\geq 1.0 \times 10^9/L$
Platelet count	$\geq 100 \times 10^9/L$
Creatinine clearance	≥ 60 mL/min
Bilirubin	$\leq 1.5 \times$ ULN
AST	$< 1.5 \times$ ULN

Dose modifications

• Haematological toxicity

If neutrophils $< 1.0 \times 10^9/L$ or platelets $< 100 \times 10^9/L$ consider 75% dose of lomustine and procarbazine.

If platelets $< 50 \times 10^9/L$ consider reducing lomustine and procarbazine to 60% dose.

In the case of febrile neutropenia (neutrophils $< 0.5 \times 10^9/L$ and fever $> 38.5^\circ C$ requiring IV antibiotics) delay until FBC recovers and consider reducing lomustine and procarbazine to 75% dose.

• Renal impairment

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

• Hepatic impairment

Bilirubin(x ULN)	Lomustine dose	Procarbazine dose	Vincristine dose
≤ 1.5	100%	100%	100%
1.5 - 3	100%	100%	50%
3 - 5	Consider dose reduction	Consider dose reduction	Omit
>5	Consider dose reduction	Contra-indicated	Omit

• Other toxicities

Toxicity	Definition	Dose adjustment
Neuropathy	Grade 2 (moderate symptoms)	Reduce procarbazine to 75% dose Reduce vincristine to 67% dose
	Grade 3+ (severe symptoms, limiting self-care)	Discontinue treatment

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.

Alcohol: Procarbazine has a weak disulfiram-like effect and can lead to alcohol intolerance.

MAO inhibition: Procarbazine is a weak inhibitor of MAO and can cause CNS side-effects. Care should be taken when co-prescribing antihypertensives, CNS depressants or tricyclic antidepressants.

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

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

- Daniels S. North London Cancer Network. Dose adjustment for cytotoxics in hepatic impairment. Accessed 19 Mar 14 via www.bopa.org.uk
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- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

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