Regimen Monograph

A - Regimen Name

PCV Regimen

Procarbazine-CCNU (Lomustine)-VinCRIStine

Disease Site
Central Nervous System

Intent
Adjuvant
Curative
Palliative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses
Adjuvant treatment following radiation therapy for grade 2 or 3 oligodendroglioma (IDH-mutant, 1p19q codeleted)

(Also refer to PEBC guideline for details on treatment recommendations.)

Supplementary Public Funding
procarbazine
ODB - General Benefit (procarbazine)

lomustine
ODB - General Benefit (lomustine)

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B - Drug Regimen

lomustine	100-110 mg /m²	PO	Day 1
procarbazine	60 mg /m²	PO	Days 8 to 21
vinCRIStine	1.4 mg /m²	IV (maximum 2 mg)	Day 8 and 29

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C - Cycle Frequency

REPEAT EVERY 42 DAYS

For a usual total of 4-6 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal (Day 29)
High (Consider prophylaxis daily for procarbazine)
Moderate (Consider prophylaxis daily for lomustine)

Febrile Neutropenia Risk: Low

Other Supportive Care:

If vomiting not controlled during procarbazine treatment, escalate antiemetic treatment – vomiting may increase intracranial pressure with larger brain tumours

Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Hematologic Toxicities:

Toxicity Type / Counts x 10^9 /L previous cycle	Procarbazine* (% previous dose)	Lomustine* (% previous dose)	Vincristine* (% previous dose)
Febrile Neutropenia Thrombocytopenic bleeding, grade 4 neutropenia or ≥ grade 3 thrombocytopenia	75%	75%	No change
Grade 2 neuropathy	75 %	No change	67%
Grade 3 neuropathy	Discontinue		
Other Grade 3 related organ	75%		
Grade 4 related organ or neurotoxicity	Discontinue		
Hypersensitivity, pneumonitis, renal failure, bronchospasm	Discontinue		

* Do not start new cycle until organ toxicity ≤ grade 2, platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L.

Hepatic Impairment

Bilirubin		AST/ALT	Procarbazine	Lomustine	Vincristine (% previous dose)
2-4 x ULN	or	2-5 x ULN	Omit	Monitor	50%
> 4 x ULN		>5 x ULN	Omit	Monitor, consider ↓	25%

Renal Impairment

Creatinine Clearance (mL/min)	Procarbazine (% previous dose)	Lomustine (% previous dose)	Vincristine (% previous dose)
>50	100%	100%	No change
10-50	75%	75%	
<10	50% or Discontinue	50% or Discontinue	

Dosage in the Elderly

Older patients may have more neurotoxicity with vincristine. No specific dosage adjustment recommended.

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F - Adverse Effects

Refer to procarbazine, lomustine, vinCRIStine drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea and vomiting • Myelosuppression (cumulative) ± bleeding, infection • CNS depression, nightmares, insomnia, hallucinations • Rash, pigmentation, radiation recall, photosensitivity • Diarrhea and stomatitis, anorexia • Neurotoxicity (cranial, peripheral ,autonomic neuropathy, disorientation, ataxia; may be severe) • Constipation, cramps (may be severe) • Fatigue, flu-like symptoms • Reproductive risks • Vesicant	• Pneumonitis / pulmonary fibrosis (may be acute or delayed) • Nephrotoxicity • Secondary leukemia, MDS • Hypersensitivity and serum sickness like reactions • Hemolytic anemia • Thromboembolism • MI, SIADH • Perforation, pancreatitis

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G - Interactions

Refer to procarbazine, lomustine, vinCRIStine drug monograph(s) for additional details.

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H - Drug Administration and Special Precautions

Refer to procarbazine, lomustine, vinCRIStine drug monograph(s) for additional details.

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Clinical toxicity assessment (including neurotoxicity, skin, CNS, local and pulmonary toxicity)
- CBC before each cycle
- Baseline and regular hepatic and renal function tests
- Pulmonary function tests with prolonged (> 6 months) therapy or cumulative lomustine doses > 1,100 mg/m^2
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Procarbazine and lomustine: Outpatient prescription for home administration

Approximate Patient Visit	Vincristine: 0.5 hour
Pharmacy Workload (average time per visit)	15.99 minutes
Nursing Workload (average time per visit)	35 minutes

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K - References

Buckner JC, Shaw EG, Pugh SL, et al. Radiation plus Procarbazine, CCNU, and Vincristine in Low-Grade Glioma. N Engl J Med 2016;374(14):1344-55.

Cairncross G, Berkey B, Shaw E, et al Phase III Trial of Chemotherapy Plus Radiotherapy Compared With Radiotherapy Alone for Pure and Mixed Anaplastic Oligodendroglioma: Intergroup Radiation Therapy Oncology Group Trial 9402. J Clin Oncol 2006;24:2707-14.

Cairncross G, Wang M, Shaw E, et al. Phase III trial of chemoradiotherapy for anaplastic oligodendroglioma: long-term results of RTOG 9402. J Clin Oncol 2013;31(3):337-43.

Mohile NA, Messersmith H, Gatson NT, et al. Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline. J Clin Oncol 2022;40(4):403-426.

Shaw EG, Wang M, Coons SW, et al: Randomized trial of radiation therapy plus procarbazine, lomustine, and vincristine chemotherapy for supratentorial adult low-grade glioma: Initial results of RTOG 9802. J Clin Oncol 2012;30:3065-70.

van den Bent MJ, Brandes AA, et al. Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC brain tumor group study 26951. J Clin Oncol 2013;31(3):344-50.

van den Bent MJ, Carpentier AF, Brandes AA, et al: Adjuvant procarbazine, lomustine, and vincristine improves progression-free survival but not overall survival in newly diagnosed anaplastic oligodendrogliomas and oligoastrocytomas: A randomized European Organisation for Research and Treatment of Cancer phase III trial. J Clin Oncol 2006;24:2715-22.

PEBC Advice Documents or Guidelines

- An Endorsement of the ASCO-SNO Guideline on Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults

January 2023 Modified Rationale/uses and Cycle frequency sections; added PEBC guideline

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on

usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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