Regimen Monograph

A - Regimen Name

TMZL Regimen

Temozolomide

Disease Site	Skin - Melanoma
Intent	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	For the treatment of patients with unresectable malignant melanoma.
Supplementary Public Funding	**temozolomide** ODB - General Benefit (temozolomide)

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B - Drug Regimen

temozolomide	200 mg /m²	PO	Days 1 to 5

(Outpatient prescription in multiples of 5mg, 20mg, 100mg, 140mg and 250mg capsules)

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate – Consider prophylaxis daily (> 75 mg/m2 OR ≤ 75 mg/m2/day + RT)
Low – No routine prophylaxis; PRN recommended (≤ 75 mg/m2/day)

Other Supportive Care:

- Screen patients for hepatitis B prior to treatment. If active, do not treat with temozolomide.
- PCP prophylaxis is required when used in combination with radiation.

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. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

Dosage with toxicity

Suggested dose levels: 200, 150 and 100 mg/m^2

Prior to treatment, ensure ANC ≥ 1.5 X 10^9/L and platelets ≥ 100 X 10^9/L.

Table 2: Modifications for worst toxicity in previous cycle					
ANC ($x10^9$/L)		**Platelets ($x10^9$/L)**		**Non-hematologic toxicity#**	**Dose for Next Cycle****
<1	OR	< 50	OR	Grade 3	Reduce by 1 dose level*
-		-		Grade 4 or Recurrent Grade 3 or pneumonitis or severe rash	Discontinue
				Hepatotoxicity	Assess risk vs. benefit before continuing treatment
				Hepatitis B	Discontinue if active disease or reactivation
# except for alopecia, nausea, vomiting * Discontinue if < $100mg/m^2$ ** New cycles of temozolomide should not be started until ANC is ≥ 1.5 x 10^9/L and platelets ≥ 100 x 10^9/L and patient has recovered from ≥ grade 3 organ toxicity.					

Female Patients

Lower clearance of temozolomide and higher incidence of grade 4 thrombocytopenia or neutropenia in females, especially in the first cycle. Monitor for toxicity.

Elderly Patients

Patients over the age of 70 years are at an increased risk of myelosuppression and should be monitored closely.

Hepatic Impairment

No formal studies have been performed. Caution should be exercised in patients with severe hepatic impairment.

Renal Impairment

No formal studies have been performed. Caution should be exercised in patients with severe renal impairment.

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F - Adverse Effects

Refer to temozolomide drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Fatigue • Alopecia • Nausea, vomiting • Anorexia, weight loss • Headache • Constipation • Myelosuppression +/- infection (including opportunistic, viral reactivation), bleeding (may be severe) • Rash (may be severe) • Diarrhea	• Arterial thromboembolism • Venous thromboembolism • Secondary malignancy • Pneumonitis • Hypersensitivity • Increased LFTs

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G - Interactions

Refer to temozolomide drug monograph(s) for additional details

- Caution and monitor for increased myelosuppression when combined with other alkylating agents.
- Caution and monitor for temozolomide toxicity when combined with valproic acid
- Caution and monitor when used with drugs that increase the risk of aplastic anemia (e.g. co-trimoxazole, carbamazepine)

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H - Drug Administration and Special Precautions

Refer to temozolomide drug monograph(s) for additional details

Administration:

- It is preferable to give temozolomide on an empty stomach, at least one hour before or at least 2 hours after a meal, as this may help reduce nausea and vomiting. Alternatively, it may be given with food; however, administration timing relative to meals should be consistent.
- Capsules must not be opened or chewed, but are to be swallowed whole with a glass of water.
- If vomiting occurs after the dose is administered, do not administer a second dose to make up for the vomited dose.
- Store capsules at room temperature (15 to 30°C).

Special precautions:

- Contraindicated in patients with hypersensitivity to temzolomide or dacarbazine, in patients with severe myelosuppression or active hepatitis B
- Use with caution in patients with hepatic impairment, poor performance status, severe debilitating diseases or infection

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- CBC; Baseline, then on day 1 and 22 of 28 day cycle
- Hepatitis B screening; Baseline. If active, do not treat with temozolomide. If not active, monitor every 1 to 2 cycles for reactivation & continue for 6 months after treatment discontinuation.
- Liver function tests; Baseline and before each cycle
- Clinical toxicity assessment including fatigue, constipation, infections (including opportunistic such as PCP and Hepatitis B), bleeding, nausea and vomiting, pneumonitis, hypersensitivity, thromboembolism, skin and respiratory toxicity; At each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for

Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Kaufmann R, Spieth K, Leiter U, et al. Temozolomide in Combination With Interferon-Alfa Versus Temozolomide Alone in Patients With Advanced Metastatic Melanoma: A Randomized, Phase III, Multicenter Study from the Dermatologic Cooperative Oncology Group. J Clin Oncol 2005; 23:9001-7.

Middleton MR, Grob JJ, Aaronson N, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. J Clin Oncol January, 2000; 18(1): 158-166.

Temozolomide drug monograph, Cancer Care Ontario.

June 2021 temozolomide is ODB General Benefit

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M - Disclaimer

Regimen Abstracts

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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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