Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

TMZL(RT)-TMZL Regimen

Temozolomide (Concurrent with Radiation and Maintenance)

Disease Site	Central Nervous System
Intent	Adjuvant 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 newly diagnosed glioblastoma multiforme, concurrently with radiation and post-radiation
Supplementary Public Funding	**temozolomide** ODB - General Benefit (temozolomide)

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B - Drug Regimen

Concurrently with Radiation:

temozolomide[1]	75 mg /m²	PO	Daily up to 6 weeks during radiotherapy

4 Weeks Post-Radiation:

temozolomide[1,2]	150-200 mg /m²	PO	Daily for 5 days

(1) PO capsules available as outpatient prescription in multiples of 5mg, 20mg, 100mg, 140mg and 250mg.
(2) Start with 150 mg/m^2 in cycle 1. For cycle 2: In absence of hematologic toxicity and ≥ grade 3 of other toxicities in cycle 1, increase to 200mg/m^2 x 5 d starting from cycle 2. Otherwise, continue with 150mg/m^2 and do not escalate dose in subsequent cycles.

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C - Cycle Frequency

Post Radiation: REPEAT EVERY 28 DAYS
For up to 6 cycles post-radiotherapy

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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:

- Antiemetic therapy is recommended prior to or following administration of temozolomide, especially for patients with emesis.
- Prophylaxis against Pneumocystis carinii pneumonia (PCP) required especially for patients during concomitant phase with radiotherapy.

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

Dose Modification for Newly Diagnosed-Concurrent RT:

- No specific dose reductions are recommended for concurrent RT phase.

Table 1: Modifications during concurrent treatment					
ANC (10^9/L)		**Platelets (**10^9/L)		**Non-hematologic toxicity#**	**Action during RT**
≥0.5 to <1.5	OR	≥10 to <100	OR	Grade 2	Hold until recovery and then restart
< 0.5	OR	<10	OR	≥ Grade 3, including pneumonitis or severe rash	Discontinue during RT
				Hepatotoxicity	Assess risk/benefit before continuing treatment
				Hepatitis B	Discontinue if active disease or reactivation
# except for alopecia, nausea, vomiting					

Dose Modifications for Adjuvant-Maintenance:

- Dose levels are 200, 150 and 100 mg/m^2

Table 2: modifications for worst toxicity in previous cycle					
ANC (10^9/L)		**Platelets (**10^9/L)		**Non-hematologic toxicity#**	**Dose for Next Cycle ****
<1	OR	< 50	OR	Grade 3	Reduce by 1 dose level*
-	OR	-	OR	Grade 4 or Recurrent Grade 3 or pneumonitis or severe rash	Discontinue
				Hepatotoxicity	Assess risk/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.

Hepatic Impairment

No formal studies have been performed. Population pharmacokinetics appear unchanged in patients with mild to moderate hepatic impairment. Patients with severe hepatic impairment should be monitored closely and consideration given to dose modification.

Renal Impairment

No formal studies have been performed. Population pharmacokinetics appear unchanged in patients with mild-moderate renal impairment. Patients with severe renal impairment should be monitored closely and consideration given to dose modification.

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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
• Myelosuppression (± infection, including opportunistic, may be severe) • Nausea and vomiting • Fatigue • Alopecia • Constipation • Headache • Anorexia • Rash (may be severe)	• Secondary malignancies • Pneumonitis/fibrosis • Arterial thromboembolism • Venous Thromboembolism • Hepatotoxicity • Hypersensitivity • Hepatitis B reactivation

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G - Interactions

Refer to temozolomide drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to temozolomide drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; Baseline then weekly for concurrent RT; Baseline then on day 1 and 22 (for q28d cycles)
- Liver function tests; Baseline then at mid-cycle (42-day cycle); Baseline then each cycle (28-day cycles)
- Hepatitis B screening; Baseline. If active, do not treat with temozolomide. If not active, monitor every 1-2 cycles for reactivation & continue for 6 months after treatment discontinuation.
- 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; Regular

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

PO: Outpatient prescription for home administration

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K - References

Temozolomide drug monograph, Cancer Care Ontario, April 2015.

Stupp R, Mason WP, Van Den Bent MJ et al. Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma. NEJM. March 10 2005; 352; 987-96.

PEBC Advice Documents or Guidelines

- Endorsement of the 2017 European Association for Neuro-Oncology Guideline on the Diagnosis and Treatment of Adult Astrocytic and Oligodendroglial Gliomas

June 2021 temozolomide is ODB General Benefit

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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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