

POLICY: Oncology – Temozolomide injection for intravenous use (Temodar® – Merck & Co, generics)

APPROVAL DATE: 08/21/2019

OVERVIEW

Temozolomide is an alkylating agent indicated in adults with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance therapy.¹ Temozolomide is also indicated in adults with refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea (i.e., BiCNU® [carmustine {BCNU} for injection] or lomustine [CCNU] capsules) and Matulane® (procarbazine capsules). Temozolomide is not directly active but undergoes rapid nonenzymatic conversion at physiologic pH to a reactive compound 5-(3-methyltriazene-1-yl)-imidazole-4-carboxamide (MTIC). The cytotoxicity of MTIC is thought to be due primarily to alkylation of DNA.

A pharmacokinetic study established bioequivalence between temozolomide 150 mg/m² administered as a 90 minute intravenous infusion and temozolomide 150 mg/m² oral administration of the capsule formulation.¹ The dose of temozolomide should be adjusted based on the nadir neutrophil and platelet counts, and the neutrophil and platelet counts prior to initiating the next cycle of therapy. Dose interruption or discontinuation is recommended for hematologic and nonhematologic toxicity, see prescribing information for more detail on dose adjustments due to toxicity.

Guidelines

The National Comprehensive Cancer Network (NCCN) Central Nervous System Cancers Clinical Practice Guidelines (version 1.2019 – March 5, 2019) note temozolomide as a treatment option for the treatment of glioblastoma multiforme and anaplastic astrocytoma.² Temozolomide is listed for use as monotherapy or as adjuvant therapy (i.e., to be used concurrently with radiation or other chemotherapeutic agents).

Other Uses with Supportive Evidence

NCCN cites the use of temozolomide as a treatment option in various cancers.

The NCCN Bone Cancer Clinical Practice Guidelines (version 2.2019 – April 10, 2019) note temozolomide as a treatment option in patients with relapsed, refractory, or metastatic Ewing's sarcoma or mesenchymal chondrosarcoma.³

The NCCN Central Nervous System (CNS) Cancers Clinical Practice Guidelines (version 1.2019 – March 5, 2019) note temozolomide as an option for a myriad of CNS cancers, including anaplastic gliomas (includes mixed anaplastic oligoastrocytoma, anaplastic oligodendroglioma, and other rare anaplastic glioma); intracranial or spinal ependymoma; gliosarcoma; primary CNS lymphoma; low-grade glioma/pilocytic and infiltrative supratentorial astrocytoma/oligodendroglioma; medulloblastoma (as recurrence therapy in patients who have tried other chemotherapeutic agents); and brain metastases from solid tumors (in patients for whom radiation therapy is not an option and who have tried other chemotherapeutic drugs that penetrate the CNS).²

The NCCN Cutaneous Melanoma Clinical Practice Guidelines (version 2.2019 – March 12, 2019) note temozolomide as a treatment option in patients with metastatic melanoma.⁴

The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines (version 1.2019 – March 5, 2019) note temozolomide as a treatment option for neuroendocrine tumors of the gastrointestinal tract, lung or thymus (carcinoid tumors); neuroendocrine tumors of the pancreas (islet cell tumors)/pancreatic neuroendocrine tumors; pheochromocytoma or paragangliomas; and neuroendocrine carcinoma (poorly differentiated, large or small cell [other than lung], unknown primary).⁵

The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines (version 2.2019 – December 17, 2018) note temozolomide as a treatment option for mycosis fungoides (MF)/ Sézary Syndrome (in patients who have tried other chemotherapeutic agents); and primary cutaneous anaplastic large cell lymphoma with multifocal lesions or regional nodes (in patients with CNS involvement).^{6,7}

The NCCN Small Cell Lung Cancer Clinical Practice Guidelines (version 1.2019 – April 9, 2019) note temozolomide as a treatment option for patients with small cell lung cancer with metastases to the brain or who have tried other chemotherapeutic agents.⁸

The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines (version 2.2019 – February 4, 2019) note temozolomide as a treatment option for angiosarcoma, rhabdomyosarcoma, solitary fibrous tumor/hemangiopericytoma; soft tissue sarcomas (in patients with advanced, unresectable, or metastatic disease who have tried other chemotherapeutic agents).⁹

The NCCN Uterine Neoplasms Clinical Practice Guidelines (version 3.2019 – February 11, 2019) note temozolomide as a treatment option for patients with metastatic, recurrent, or medically inoperable uterine sarcoma.¹⁰

The NCCN Uveal Melanoma Clinical Practice Guidelines (version 1.2019 – June 14, 2019) note temozolomide as a treatment option for patients with metastatic or unresectable uveal melanoma.¹¹

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of temozolomide. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Because of the specialized skills required for evaluation and diagnosis of patients treated with temozolomide as well as the monitoring required for adverse events and long-term efficacy, approval requires temozolomide to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of temozolomide intravenous is recommended in those who meet the following criteria:

FDA-Approved Indications

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1. **Glioblastoma multiforme (GBM, Glioblastoma, Grade IV Astrocytoma).** Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Initial (Concomitant) Phase: Administer up to 75 mg/m² intravenously daily for up to 49 days;
OR
B) Maintenance Phase: Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle.¹

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2. **Anaplastic Astrocytoma.** Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle.¹

Other Uses with Supportive Evidence

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3. **Anaplastic Gliomas (Includes Mixed Anaplastic Oligoastrocytoma, Anaplastic Oligodendroglioma, and Other Rare Anaplastic Gliomas).** Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle;¹²⁻¹⁴ OR
B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.^{15,16}

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4. **Angiosarcoma.** Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle.²⁷⁻²⁹

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5. **Brain Metastases from Solid Tumors.** Approve for 6 months if the patient meets the following criteria (A, B, and C):

- A) Radiation therapy is not an option; AND
B) At least one chemotherapy drug that penetrates the central nervous system (e.g., cyclophosphamide/methotrexate [MTX]/fluorouracil for breast cancer; carboplatin and etoposide for non-small cell lung cancer [NSCLC]) has already been tried; AND
C) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle; OR
B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle; OR

C) Administer up to 75 mg/m² intravenously daily for up to 42 days of each 56-day cycle.³²

6. Ependymoma, Intracranial or Spinal. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle.³³

7. Ewing's Sarcoma or Mesenchymal Chondrosarcoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has relapsed, refractory, or metastatic disease; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 150 mg/m² intravenously for up to 5 days of each 21-day cycle.²⁴⁻²⁶

8. Gliosarcoma. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Initial (Concomitant) Phase: Administer up to 75 mg/m² intravenously daily for up to 49 days; OR
- B) Maintenance Phase: Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle.¹

9. Low-Grade (WHO Grade I or II) Glioma/Pilocytic and Infiltrative Supratentorial Astrocytoma/Oligodendroglioma in Adults. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):

- A) Administer up to 75 mg/m² intravenously daily for up to 49 days of each 77-day cycle;¹⁷ OR
- B) Administer up to 75 mg/m² intravenously daily for up to 21 days of each 28-day cycle;¹⁸ OR
- C) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle.¹⁹⁻²²

10. Medulloblastoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has received prior chemotherapy; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days in each 21-day or 28-day cycle.³⁴⁻³⁶

11. Melanoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has metastatic disease; AND

B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle; OR
- B) Administer up to 75 mg/m² intravenously daily for up to 42 days of each 56-day cycle; OR
- C) Administer up to 75 mg/m² intravenously daily for up to 21 days of each 28-day cycle.³⁷

12. Mycosis Fungoides/Sezary Syndrome. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has received one prior therapy; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist or dermatologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle.³⁸⁻³⁹

13. Neuroendocrine Tumors of the Gastrointestinal Tract, Lung or Thymus (Carcinoid Tumors).

Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle;^{40,41} OR
- B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.^{42,43}

14. Neuroendocrine Tumors of the Pancreas (Islet Cell Tumors), Pancreatic Neuroendocrine Tumors. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle;^{44,45} OR
- B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.^{42,46}

15. Neuroendocrine Carcinoma – Poorly Differentiated, Large or Small Cell (Other than Lung), Unknown Primary. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle;⁴⁷ OR
- B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.⁴²

16. Pheochromocytoma or Paragangliomas. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has metastases; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle;⁴⁸ OR
- B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.⁴³

17. Primary Central Nervous System Lymphoma. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days in each 21-day or 28-day cycle.⁴⁹⁻⁵²

18. Primary Cutaneous Anaplastic Large Cell Lymphoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has relapsed/refractory disease with central nervous system involvement; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle.³⁸⁻³⁹

19. Rhabdomyosarcoma. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m² intravenously daily for up to 5 days of each 21-day or 28-day cycle.²⁵⁻²⁷

20. Small Cell Lung Cancer. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has one of the following (i or ii):
 - i. The patient has tried one chemotherapy regimen; OR
 - ii. The patient has metastases to the brain; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days in each 28-day cycle;^{53,54} OR
- B) Administer up to 75 mg/m² intravenously daily for up to 21 days of each 28-day cycle.⁵⁵

21. Soft Tissue Sarcoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has advanced, unresectable, or metastatic disease; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days of each 21-day or 28-day cycle;²⁵⁻²⁹ OR
- B) Administer up to 100 mg/m² intravenously daily for up to 21 days of each 28-day cycle;³⁰ OR
- C) Administer up to 100 mg/m² intravenously daily for up to 42 days of each 63-day cycle.³¹

22. Solitary Fibrous Tumor/Hemangiopericytoma. Approve for 6 months if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.²³

23. Uterine Sarcoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has metastatic, recurrent, or medically inoperable disease; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):

- A) Administer up to 200 mg/m² intravenously daily for up to 5 days of each 28-day cycle;²⁹ OR
- B) Administer up to 100 mg/m² intravenously daily for up to 21 days of each 28-day cycle;³⁰ OR
- C) Administer up to 100 mg/m² intravenously daily for up to 42 days of each 63-day cycle.³¹

24. Uveal Melanoma. Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has metastatic or unresectable disease; AND
- B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):

- A) Administer up to 75 mg/m² intravenously daily for up to 21 days of each 28-day cycle;⁵⁶ OR
- B) Administer up to 150 mg/m² intravenously daily for up to 14 days of each 28-day cycle.⁵⁷

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Temozolomide has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Approval Date
New Policy	--	08/21/2019

