

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Temozolomide capsules (Temodar® – Merck & Co, generic)

TAC APPROVAL DATE: 07/17/2019

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-methyltriazen-1-yl)-imidazole-4-carboxamide (MTIC). The cytotoxicity of MTIC is thought to be due primarily to alkylation of DNA.

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 prescription benefit coverage of temozolomide capsules. All approval durations are for 3 years.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

- 1. Glioblastoma multiforme (GBM, Glioblastoma, Grade IV Astrocytoma).** Approve for 3 years.
- 2. Anaplastic Astrocytoma.** Approve for 3 years.

Other Uses with Supportive Evidence

- 3. Anaplastic Gliomas (Includes Mixed Anaplastic Oligoastrocytoma, Anaplastic Oligodendroglioma, and Other Rare Anaplastic Gliomas).** Approve for 3 years.
 - 4. Angiosarcoma.** Approve for 3 years.
 - 5. Brain Metastases from Solid Tumors.** Approve for 3 years if the patient meets the following criteria (A and B):
 - A)** Radiation therapy is not an option; AND
 - B)** Other chemotherapy drugs that penetrate the central nervous system (e.g., cyclophosphamide/methotrexate [MTX]/fluorouracil for breast cancer; carboplatin and etoposide for non-small cell lung cancer [NSCLC]) have already been tried.
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6. **Ependymoma, Intracranial or Spinal.** Approve for 3 years.
 7. **Ewing's Sarcoma or Mesenchymal Chondrosarcoma.** Approve for 3 years in patients with relapsed, refractory or metastatic disease.
 8. **Gliosarcoma.** Approve for 3 years.
 9. **Low-Grade (WHO Grade I or II) Glioma/ Pilocytic and Infiltrative Supratentorial Astrocytoma/Oligodendroglioma in Adults.** Approve for 3 years.
 10. **Medulloblastoma.** Approve for 3 years for recurrence therapy in patients who have received prior chemotherapy.
 11. **Melanoma.** Approve for 3 years if the patient has metastatic melanoma.
 12. **Mycosis Fungoides/Sézary Syndrome.** Approve for 3 years in patients who have received one prior therapy.
 13. **Neuroendocrine Tumors of the Gastrointestinal Tract, Lung or Thymus (Carcinoid Tumors).** Approve for 3 years.
 14. **Neuroendocrine Tumors of the Pancreas (Islet Cell Tumors), Pancreatic Neuroendocrine Tumors.** Approve for 3 years.
 15. **Neuroendocrine Carcinoma – Poorly Differentiated, Large or Small Cell (Other than Lung), Unknown Primary.** Approve for 3 years.
 16. **Pheochromocytoma or Paragangliomas.** Approve for 3 years in patients with metastases.
 17. **Primary Central Nervous System Lymphoma.** Approve for 3 years.
 18. **Primary Cutaneous Anaplastic Large Cell Lymphoma** Approve for 3 years in patients with relapsed/refractory disease with central nervous system involvement.
 19. **Rhabdomyosarcoma.** Approve for 3 years.
 20. **Small Cell Lung Cancer.** Approve for 3 years if the patient meets ONE of the following criteria (A or B):
 - A) The patient has tried one chemotherapy regimen; OR
 - B) The patient has metastases to the brain.
 21. **Soft Tissue Sarcomas.** Approve for 3 years in patients with advanced, unresectable, or metastatic disease.
 22. **Solitary Fibrous Tumor/Hemangiopericytoma.** Approve for 3 years.
 23. **Uterine Sarcomas.** Approve for 3 years in patients with metastatic, recurrent or medically inoperable disease.
 24. **Uveal Melanoma.** Approve for 3 years for metastatic or unresectable disease.
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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. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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

REFERENCES

1. Temodar® capsules [prescribing information]. White Station, NJ: Merck & Co., Inc (manufactured by Baxter Oncology GmbH, Halle, Germany); September 2015.
2. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (Version 1.2019 – March 5, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 17, 2019.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (Version 2.2019 – April 10, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 24, 2019.
4. The NCCN Cutaneous Melanoma Clinical Practice Guidelines in Oncology (Version 2.2019 – March 12, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 17, 2019.
5. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (Version 1.2019 – March 5, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 17, 2019.
6. The NCCN Primary Cutaneous Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – December 17, 2018). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 24, 2019.
7. The NCCN Drugs & Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 25, 2018. Search terms: temozolomide.
8. The NCCN -Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 1.2019 – April 9, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 17, 2019.
9. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (Version 2.2019 – February 4, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 24, 2019.
10. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (Version 3.2019 – February 11, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 17, 2019.
11. The NCCN Uveal Melanoma Clinical Practice Guidelines in Oncology (Version 1.2019 – June 14, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 24, 2019.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Melanoma criteria were revised to remove the criterion requiring targeted therapy if the patient's melanoma is BRAF V600 mutation positive. Head/Neck was added to the Soft Tissue Sarcomas indication. The indication Uterine Leiomyosarcoma or High Grade Endometrial Sarcoma was revised to say Uterine Sarcoma and list the more specific uses. The criteria requiring adjuvant use after trying doxorubicin or gemcitabine plus docetaxel was removed. Criterion for a new indication, Pheochromocytoma or Paragangliomas, was added.	04/20/2016
Annual revision	Due to NCCN terminology, "Carcinoid Tumors" indication is now changed to "Neuroendocrine Tumors of the Lung and Thymus" with "(Carcinoid Tumors)" noted in parentheses. Removed "Gastrointestinal Tract" from the above indication since temozolomide is used only in lung and thymus. Deleted descriptor of "unresectable, advanced" from Melanoma indication and "Advanced" from Neuroendocrine Tumors of the Pancreas. Added "or Mesenchymal Chondrosarcoma" to Ewing's Sarcoma indication since the guidelines recommend following same treatment pathway for Mesenchymal Chondrosarcoma.	06/07/2017
Annual revision	Added new approval conditions for Uveal Melanoma and Neuroendocrine Carcinomas – Poorly Differentiated, Large or Small cell (Other than Lung), Unknown Primary. Deleted the following approval conditions from Other Uses	06/27/2018

	with Supportive Evidence section: Patient has been started on temozolomide and Dermatofibrosarcoma Protuberans (DFSP). Also deleted “Supratentorial Primitive Neuroectodermal Tumor” from Medulloblastoma approval condition.	
Annual revision	Revisions: • Low-Grade (WHO Grade I or II) Glioma/ Pilocytic and Infiltrative Supratentorial Astrocytoma/Oligodendroglioma in Adults: The condition of approval was changed to as listed to address pilocytic astrocytoma. Previously, it was listed as Low-Grade Infiltrative Supratentorial Astrocytoma/Oligodendroglioma (excluding pilocytic astrocytoma) in Adults • Mycosis Fungoides/ Sezary Syndrome: Criteria were revised to require one prior therapy and examples were removed. Previously, one prior chemotherapy was required and several examples were listed. • Neuroendocrine Tumors of the Gastrointestinal Tract, Lung or Thymus (Carcinoid Tumors): This condition of approval was changed to as listed. Previously, it was listed as Neuroendocrine Tumors of the Lung or Thymus (carcinoid tumors). • Small Cell Lung Cancer: The list of chemotherapy examples was removed. • Soft Tissue Sarcomas: This condition of approval was changed to as listed. Previously, it was listed as Soft Tissue Sarcomas of the Extremities, Superficial Trunk, Head/Neck, or Retroperitoneal/Intra-Abdominal Soft Tissue Sarcomas. The requirement of a trial of one other chemotherapy (single or combination) was removed as it is no longer supported in the National Cancer Center Network (NCCN) guidelines. • Uterine Sarcomas: The condition of approval was changed to as listed. Previously, it was listed as Uterine Sarcoma (i.e., High-Grade Endometrial Stromal Sarcoma, Undifferentiated Uterine Sarcoma, Uterine Leiomyosarcoma). • Primary Cutaneous Large Cell Lymphoma: The new condition of approval was added. Criteria are to approve for 3 years in patients with relapsed/refractory disease with central nervous system involvement.	07/17/2019

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a summary of criteria changes, refer to TAC respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.