Clinical Policy: Temozolomide (Temodar)

Reference Number: CP.PHAR.77
Effective Date: 09.01.11
Last Review Date: 05.25
Line of Business: HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Temozolomide (Temodar®) is an imidazotetrazine derivative.

FDA Approved Indication(s)

Temodar is indicated for the treatment of:

- Adults with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment.
- Adjuvant treatment of adults with newly diagnosed anaplastic astrocytoma.
- Adults with refractory anaplastic astrocytoma.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that temozolomide and Temodar are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Glioblastoma or Astrocytoma (must meet all):

1. Diagnosis of glioblastoma† or isocitrate dehydrogenase (IDH)-mutant astrocytoma (*see Appendix D*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For IDH-mutant astrocytoma, disease is World Health Organization (WHO) grade 2, 3, or 4;
5. Member must use generic temozolomide, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed (i or ii):
      i. Glioblastoma: 75 mg/m^2 per day for the first 42 consecutive days, followed by 200 mg/m^2 per day on days 1-5 of each 28-day cycle;
      ii. IDH-mutant astrocytoma: 200 mg/m^2 per day on days 1-5 of each 28-day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

[†] *A high-grade WHO grade IV glioma also known as glioblastoma*

B. NCCN Compendium Supported Uses (off-label) (must meet all):
1. Prescribed for one of the following NCCN category 1 or 2A recommended indications (a - l):
   a. Ewing sarcoma in combination with irinotecan for relapsed or progressive disease;
   b. Cutaneous melanoma as subsequent therapy for metastatic or unresectable disease if not eligible for immunotherapy or target therapy options;
   c. One of the following neuroendocrine or adrenal tumors (i, ii, or iii):
      i. Gastrointestinal tract, pancreas, lung, thymus, or pheochromocytoma/paraganglioma;
      ii. Extrapulmonary poorly differentiated neuroendocrine carcinoma, large or small cell carcinoma, mixed neuroendocrine-non-neuroendocrine neoplasms;
      iii. Well-differentiated grade 3 neuroendocrine tumors;
   d. Neuroblastoma in combination with irinotecan, Unituxin® (dinutuximab), and Leukine® (sargramostim);
   e. Small cell lung cancer as subsequent systemic therapy;
   f. Soft tissue sarcoma as palliative treatment for retroperitoneal/intra-abdominal disease, pleomorphic rhabdomyosarcoma, extremity/superficial trunk (body wall) disease, and head/neck disease;
   g. Nonpleomorphic rhabdomyosarcoma in combination with vincristine and irinotecan;
   h. Solitary fibrous tumor in combination with bevacizumab;
   i. Mycosis fungoides/Sézary syndrome, as subsequent systemic therapy;
   j. Advanced, recurrent/metastatic, or inoperable uterine sarcoma, as second-line or subsequent therapy;
   k. Metastatic or unresectable uveal melanoma;
   l. One of the following central nervous system cancers (i-viii):
      i. Pediatric diffuse high-grade gliomas;
      ii. Pediatric medulloblastoma for recurrent or progressive disease;
      iii. Oligodendroglioma (WHO grade II or III, IDH-mutant, 1p19q codeleted), as adjuvant treatment or treatment for recurrent or progressive disease;
      iv. Recurrent or progressive circumscribed glioma;
      v. Primary CNS lymphoma;
      vi. Brain metastases;
      vii. Intracranial and spinal ependymoma for disease progression or recurrence;
      viii. Medulloblastoma for disease recurrence;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years (all indications except for pediatric diffuse high-grade gliomas and pediatric medulloblastoma);
4. Member must use generic temozolomide, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 200 mg/m^2 per day on days 1-5 of each 28-day cycle;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Temodar for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member must use generic temozolomide, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 200 mg/m^2 per day on days 1-5 of each 28-day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CNS: central nervous system
FDA: Food and Drug Administration
IDH: isocitrate dehydrogenase
NCCN: National Comprehensive Cancer Network
RT: radiotherapy
WHO: World Health Organization

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to temozolomide or any other ingredients in Temodar and dacarbazine
- Boxed warning(s): none reported

Appendix D: General Information

- The NCCN CNS (version 2.2022) guideline no longer uses the terminology "anaplastic" to describe CNS tumors; anaplastic has been replaced with tumor specific terminology (e.g., IDH-mutant astrocytoma, IDH mutant, 1p19q codeleted oligodendroglioma).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Glioblastoma multiforme	*Concomitant phase:* 75 mg/m^2 daily for 42 days concomitant with focal radiotherapy (RT) (60 Gy administered in 30 fractions) followed by maintenance Temodar for 6 cycles. *Maintenance phase:* • *Cycle 1:* Four weeks after completing the Temodar + RT phase, Temodar is administered for an additional 6 cycles of maintenance treatment. Dosage in Cycle 1 (maintenance) is 150 mg/m^2 once daily for 5 days followed by 23 days without treatment.	200 mg/m^2/day

Indication	Dosing Regimen	Maximum Dose
	• *Cycles 2-6:* At the start of Cycle 2, the dose can be escalated to 200 mg/m^2. The dose remains at 200 mg/m^2 per day for the first 5 days of each subsequent cycle except if toxicity occurs. If the dose was not escalated at Cycle 2, escalation should not be done in subsequent cycles.	
IDH-mutant astrocytoma	Adjuvant treatment for newly diagnosed anaplastic astrocytoma: Beginning 4 weeks after the end of RT, administer once daily for 5 consecutive days per 28-day treatment cycle for 12 cycles. Dosage of Cycle 1 is 150 mg/m^2. The dose should be increased to 200 mg/m^2 per day if no or minimal toxicity is experienced in Cycle 1. Refractory anaplastic astrocytoma: Initial dose is 150 mg/m^2 once daily for 5 consecutive days per 28-day treatment cycle. The dose should be increased to 200 mg/m^2 if absolute neutrophil count is ≥ 1.5 x 10^9/L and platelet count is ≥ 100 x 10^9/L. Continue Temodar until disease progression or unacceptable toxicity. In the clinical trial, treatment could be continued for a maximum of 2 years, but the optimum duration of therapy is not known.	200 mg/m^2/day

VI. Product Availability

- Intravenous reconstituted solution (Temodar): 100 mg
- Oral capsules (Temodar, generic): 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, 250 mg

VII. References

1. Temodar Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; September 2023. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022277s017_018_019lbl.pdf. Accessed January 28, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed January 28, 2025.
3. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: A summary. *Acta Neuropathologica.* June 2016; 131(6): 803-820.
4. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 4.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed January 28, 2025.

5. National Comprehensive Cancer Network. Pediatric Central Nervous System Cancers Version 2.2025. Available https://www.nccn.org/professionals/physician_gls/pdf/ped_cns.pdf. Accessed January 28, 2025.
6. National Comprehensive Cancer Network. Central Nervous System Cancers Version 4.2024. Available https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed January 28, 2025.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J8700	Temozolomide, oral, 5 mg
J9328	Injection, temozolomide, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added anaplastic glioma as an off-label NCCN-supported category 2A indication; modified the following off-label indications to align with NCCN recommended category 1 or 2A ratings: brain metastases, small cell lung cancer, pleomorphic rhabdomyosarcoma, solitary fibrous tumor, uterine sarcoma, and uveal melanoma; removed off-label indication of primary cutaneous anaplastic large cell lymphoma as this is no longer supported by NCCN; revised requirement of medical justification for inability to use generic temozolomide to "must use" language and added it to continued therapy criteria; contraindications added in Appendix C; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	02.20.21	05.21
Clarified dosing requirements per FDA label, including that maintenance doses should only be administered on days 1-5 of each 28 day cycle).	06.14.21	
2Q 2022 annual review: Per NCCN, added indication of low-grade (WHO grade 1 or II) recurrent or progressive glioma, removed "recurrent" from brain metastases indication, added mucosal melanoma, modified cutaneous melanoma indication use from second line to subsequent therapy, and added neuroendocrine tumor of the lung; WCG.CP.PHAR.77 was retired and initial approval duration was consolidated to 6 months; references reviewed and updated.	02.18.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	
2Q 2023 annual review: for astrocytoma, replaced term anaplastic (no longer used in compendium) with IDH mutant per NCCN, added WHO	02.24.23	05.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
grading per NCCN, added "disease is refractory and progressive despite treatment with procarbazine and nitrosourea" and added Appendix B per FDA label; per NCCN, removed criteria for mucosal melanoma (downgraded to 2B recommendation) and angiosarcoma as use is no longer recommended, updated off label-use criteria for solitary fibrous tumor to require use with bevacizumab, added off-label criteria for extrapulmonary poorly differentiated neuroendocrine carcinoma, large or small cell carcinoma, mixed neuroendocrine-non-neuroendocrine neoplasms, pediatric diffuse high-grade gliomas, updated off-label criteria for astrocytoma, oligodendroglioma and uterine sarcoma to align with NCCN; references reviewed and updated.		
RT4: for anaplastic astrocytoma removed criteria for refractory disease to reflect revised indications for newly diagnosed anaplastic astrocytoma and refractory anaplastic astrocytoma; removed Appendix B per revised FDA label; per NCCN added off-label criteria for pediatric diffuse midline gliomas; references reviewed and updated.	10.02.23	
2Q 2024 annual review: added generic temozolomide to policy/criteria section given formulary and prior authorization status;for off-label NCCN Compendium, added unresectable uveal melanoma, added neuroblastoma in combination with irinotecan, dinutuzimab, and sargramostim, revised recurrent or progressive low-grade glioma to circumscribed glioma; references reviewed and updated.	02.22.24	05.24
2Q 2025 annual review: for off-label NCCN Compendium, added criteria for well-differentiated grade 3 neuroendocrine tumors, added criteria for pediatric medulloblastoma, revised the following off-label indications to align with NCCN recommended category 1 or 2A ratings: cutaneous melanoma, pediatric diffuse high-grade gliomas, intracranial and spinal ependymoma, and medulloblastoma; references reviewed and updated.	01.28.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.