Clinical Policy: Temozolomide (Temodar)

Reference Number: CP.PHAR.77
Effective Date: 09.01.11
Last Review Date: 05.21
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:

- Adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment
- Adult patients with refractory anaplastic astrocytoma, i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine

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 Temodar is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Glioblastoma or Anaplastic Astrocytoma (must meet all):

1. Diagnosis of glioblastoma† or anaplastic astrocytoma**;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
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 (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. Anaplastic 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 multiforme (GBM)*
*** A high-grade WHO grade III glioma*

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 - p):
   a. Ewing sarcoma in combination with irinotecan for relapsed or progressive disease
   b. Intracranial and spinal ependymoma for disease progression
   c. Medulloblastoma as a single-agent for recurrence in patients who received prior chemotherapy;
   d. Low-grade (WHO grade II) infiltrative supratentorial astrocytoma/oligodendroglioma;
   e. Anaplastic glioma (WHO grade III);
   f. Primary CNS lymphoma;
   g. Brain metastases for recurrent disease;
   h. Cutaneous melanoma as second-line therapy for metastatic or unresectable disease, or after disease progression or maximum clinical benefit from BRAF targeted therapy;
   i. Neuroendocrine tumors of the gastrointestinal tract, pancreas, thymus, or pheochromocytoma/paraganglioma;
   j. Small cell lung cancer as subsequent systemic therapy;
   k. Soft tissue sarcoma as palliative treatment for retroperitoneal/intra-abdominal disease, angiosarcoma, pleomorphic rhabdomyosarcoma, extremity/superficial trunk disease, and head/neck disease;
   l. Soft tissue sarcoma for nonpleomorphic rhabdomyosarcoma in combination with vincristine and irinotecan;
   m. Soft tissue sarcoma for solitary fibrous tumor;
   n. Mycosis fungoides/Sézary syndrome;
   o. Recurrent or metastatic uterine sarcoma;
   p. Metastatic uveal melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
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

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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 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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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
GBM: glioblastoma multiforme
NCCN: National Comprehensive Cancer Network
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

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 (60 Gy	200 mg/m^2/day

Indication	Dosing Regimen	Maximum Dose
	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. • *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.	
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 $\geq$ 1.5 x 10^9/L and platelet count is $\geq$ 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.; November 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021029s033lbl.pdf. Accessed June 14, 2021.
2. Temozolomide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed June 14, 2021.
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.

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
Glioblastoma adjuvant treatment for 12 cycles post radiotherapy is decreased to 6 cycles. Maximum dose added for both indications. Off-label coverage is limited to NCCN uses categorized as 1 or 2a (2b is removed). For anaplastic astrocytoma: Off-label use as a single agent is limited to positive identification of 1p19q uni- or non-deleted tumor status. Safety information is removed. Renewal periods are increased from 6 to 12 months. HCPCS codes updated	07.17	08.17
Typo fixed to allow coverage for anaplastic astrocytoma to match FDA approved indication for the treatment of disease that has progressed on a drug regimen containing nitrosourea or procarbazine. Previous policy indicated indicated use in disease that has progressed on nitrosourea and procarbazine	12.17	
2Q 2018 annual review: added HIM line of business; added age; added continuity of care language; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; updated NCCN Compendium supported uses; references reviewed and updated.	02.08.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.05.19	05.19
2Q 2020 annual review: updated NCCN compendium-supported uses; condensed similar criteria for glioblastoma and anaplastic astrocytoma; added requirement for medical justification if brand Temodar requested as generic is available; references reviewed and updated.	02.15.20	05.20
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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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	

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.

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.