Clinical Policy: Temozolomide (Temodar)

Reference Number: CP.PHAR.77
Effective Date: 09.01.11
Last Review Date: 05.20
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. If brand Temodar is requested, medical justification supports inability to use generic temozolomide (e.g., contraindication to excipients in temozolomide);
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 200 mg/m^2 per day;
   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. Ewing sarcoma in combination with irinotecan for relapsed or progressive disease

b. Adult intracranial and spinal ependymoma for disease progression
c. Adult medulloblastoma as a single-agent for recurrence in patients who received prior chemotherapy;
d. Low-grade (WHO grade II) infiltrative supratentorial astrocytoma/oligodendroglioma;
e. Primary CNS lymphoma;
f. Brain metastases for recurrent disease if active against primary tumor;
g. Melanoma as second-line therapy for metastatic or unresectable disease, or after disease progression or maximum clinical benefit from BRAF targeted therapy;
h. Neuroendocrine tumors of the gastrointestinal tract, pancreas, thymus, or pheochromocytoma/paraganglioma;
i. Small cell lung cancer in primary progressive disease or with relapse within 6 months following complete or partial response or stable disease with initial treatment;
j. Soft tissue sarcoma as palliative treatment for retroperitoneal/intra-abdominal disease, angiosarcoma, rhabdomyosarcoma, extremity/superficial trunk disease, and head/neck disease;
k. Soft tissue sarcoma for nonpleomorphic rhabdomyosarcoma in combination with vincristine and irinotecan;
l. Soft tissue sarcoma for solitary fibrous tumor and hemangiopericytoma in combination with bevacizumab;
m. Mycosis fungoides/Sézary syndrome;
n. Primary cutaneous anaplastic large cell lymphoma for recurrence in patients who received prior chemotherapy;
o. Uterine sarcoma;
p. Uveal melanoma;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If brand Temodar is requested, medical justification supports inability to use generic temozolomide (e.g., contraindication to excipients in temozolomide);
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 200 mg/m^2 per day;
   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.PHAR.21 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. 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;
   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.PHAR.21 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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
CNS: central nervous system
NCCN: National Comprehensive Cancer Network
WHO: World Health Organization

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Avastin® (bevacizumab)	**Glioblastoma and Anaplastic Astrocytoma** Varies upon protocol and patient tolerance	Varies
Nitrosoureas* (e.g., carmustine, fotemustine, lomustine)	**Anaplastic Astrocytoma** Varies upon protocol and patient tolerance	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
procarbazine hydrochloride*	**Anaplastic Astrocytoma** Varies upon protocol and patient tolerance	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Example of a regimen containing a nitrosourea and procarbazine: PCV (procarbazine, lomustine, vincristine).*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Glioblastoma multiforme	*Concomitant phase:* 75 mg/m2 daily for 42 days concomitant with focal radiotherapy (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. *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.	200 mg/m^2/day
Anaplastic astrocytoma	Initial dose is 150 mg/m^2 once daily for 5 consecutive days per 28-day treatment cycle.	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 February 15, 2020.
2. Temozolomide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed February 15, 2020.
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
Policy converted to new template. CBC, LFT, HBV screening requirements removed. Evidence of HBV infection removed as reason to discontinue; remaining reasons to discontinue are separated per indication. Glioblastoma: Toxicity criteria is restricted to continuation of therapy – footnote added defining Grades 3 and 4. Approved number of FDA labeled adjuvant cycles (after Temodar/radiotherapy) is increased from 6 to 12 cycles total. "No disease progression" is added under continuation criteria. All NCCN compendial uses added; NCCN glioblastoma and anaplastic astrocytoma criteria are outlined in section I. Initial policy approval periods are increased to 6 months.	07.16	08.16
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;	02.15.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
added requirement for medical justification if brand Temodar requested as generic is available; references reviewed and updated.		

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.