Clinical Policy: Temozolomide (Temodar)

Reference Number: PA.CP.PHAR.77
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

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
It is the policy of Pennsylvania Health and Wellness ® that Temodar (IV brand/PO brand and generic) is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Glioblastoma (must meet all):

1. Diagnosis of glioblastoma*:
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 200 mg/m^2/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*)._____

**A high-grade WHO grade IV glioma also known as glioblastoma multiforme (GBM).*

Approval duration: 6 months

B. Anaplastic Astrocytoma (must meet all):

1. Diagnosis of anaplastic astrocytoma*;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 200 mg/m^2/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**A high-grade WHO grade III glioma.*

Approval duration: 6 months

C. 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 as a single-agent for disease progression
c. Adult medulloblastoma as a single-agent for recurrence in patients who received prior chemotherapy;
d. Primary CNS lymphoma;
e. Melanoma as second-line therapy for metastatic or unresectable disease, or after disease progression or maximum clinical benefit from BRAF targeted therapy;
f. Neuroendocrine tumors of the gastrointestinal tract, pancreas, or pheochromocytoma/paraganglioma
g. 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;
h. Soft tissue sarcoma as palliative treatment for retroperitoneal/intra-abdominal disease, angiosarcoma, and rhabdomyosarcoma;
i. Soft tissue sarcoma for nonpleomorphic rhabdomyosarcoma in combination with vincristine and irinotecan;
j. Soft tissue sarcoma for solitary fibrous tumor and hemangiopericytoma in combination with bevacizumab;
k. Mycosis fungoides/Sézary syndrome;
l. Uterine sarcoma;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 200 mg/m^2/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);
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/day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. 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
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).*

IV. 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,	200 mg/m^2/day

Indication	Dosing Regimen	Maximum Dose
	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.	200 mg/m^2/day

V. Product Availability

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

VI. References

1. Temodar Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; October 2017. Available at https://www.merck.com/product/usa/pi_circulars/t/temodar_capsules/temodar_pi.pdf. Accessed February 5, 2019.
2. Temozolomide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed February 8, 2018.
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	Approval Date
2Q 2019 annual review: no significant changes; references reviewed and updated.	04-19	