Clinical Policy: Temozolomide (Temodar)

Reference Number: ERX.SPA.138
Effective Date: 03.01.14
Last Review Date: 05.21
Line of Business: Commercial, Medicaid

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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:
Commercial – Length of Benefit
Medicaid – 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:
Commercial – Length of Benefit
Medicaid – 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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:
Commercial – Length of Benefit
Medicaid – 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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. 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.; 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Age added. Glioblastoma adjuvant treatment for 12 cycles post radiotherapy is decreased to 6 cycles per PI and based on the NCCN observation that benefit beyond 6 cycles is unknown (NCCN does note however that treatment for 12 cycles is becoming more common). Anaplastic astrocytoma: Nitrosourea examples are added. Off-label use as a single agent is limited to positive identification of 1p19q uni- or non-deleted tumor status per NCCN category 2a. Maximum dose added for both indications. Dosing guidance for off-label use added. All off-label uses are referred to the off-label use policy. Renewal periods are increased from 6 to 12 months. References updated.	07.17	08.17
2Q 2018 annual review: summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement; references reviewed and updated; added NCCN Compendium supported uses to Section I; approval durations changed to length of benefit; 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; added requirement for medical justification if brand Temodar requested as generic is available; added Medicaid line of business with 6/12 month approval durations; 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 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	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.