

Clinical Policy: Temozolomide (Temodar)

Reference Number: ERX.SPA.138

Effective Date: 03.01.14

Last Review Date: 05.20

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 \geq 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/m² 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:

Commercial – Length of Benefit

Medicaid – 6 months

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

***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 \geq 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/m² 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:

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. If request is for a dose increase, request meets one of the following (a or b):*
 - a. New dose does not exceed 200 mg/m² 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:

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

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 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Glioblastoma multiforme	<i>Concomitant phase:</i> 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. <i>Maintenance phase:</i> <ul style="list-style-type: none"> • <i>Cycle 1:</i> 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/m² once daily for 5 days followed by 23 days without treatment. <i>Cycles 2-6:</i> 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy converted to new template. Removed all safety criteria. All NCCN compendial uses added; NCCN glioblastoma and anaplastic astrocytoma criteria are outlined in section. Modified approval duration to 3 months for initial and 6 months for re-auth. Glioblastoma initial criteria: Approved number of adjuvant cycles under section I.A.2.a is increased to 12 cycles per NCCN/UpToDate notation that administering 12 cycles is an increasingly common practice.	08.16	09.16
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

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.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2014 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.