Clinical Policy: Temozolomide (Temodar)
Reference Number: ERX.SPMN.53
Effective Date: 03/14
Last Review Date: 09/16

See Important Reminder at the end of this policy for important regulatory and legal information.

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that temozolomide (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):
      *A high-grade glioma classified as astrocytoma WHO grade IV and also known by the older term glioblastoma multiforme (GBM).
      1. Diagnosis of glioblastoma (histologic variants include giant cell glioblastoma, small cell glioblastoma, gliosarcoma, and glioblastoma with oligodendroglioma component);
      2. Temodar will be used for one of the following indications:
         a. FDA approved use (i or ii):
            i. Newly diagnosed glioblastoma multiforme concomitantly with radiotherapy (up to 49 days) with concomitant pneumocystis pneumonia prophylaxis;
            ii. As maintenance therapy following concomitant temozolomide/radiotherapy;
         b. Off-label NCCN recommended use (i or ii):
            i. Adjuvant treatment as a single agent following resection for tumors that are methylguanine methyl-transferase (MGMT) promotor methylated;
            ii. Treatment of recurrent disease as a single agent or in combination with bevacizumab.

   Approval duration: 3 months

   B. Anaplastic Astrocytoma* (must meet all):
      *A high-grade anaplastic glioma classified as anaplastic astrocytoma WHO grade III.
      1. Diagnosis of anaplastic astrocytoma;
      2. Member meets a or b:
         a. FDA approved use for treatment of refractory anaplastic astrocytoma for those who have failed a drug regimen containing nitrosourea and procarbazine;
         b. Off-label NCCN recommended use:
            i. Treatment of recurrent disease as a single agent or in combination with bevacizumab;
            ii. Adjuvant treatment in combination with radiotherapy for 1p19q uni- or non-deleted anaplastic astrocytoma;
iii. Adjuvant treatment as a single-agent.

Approval duration: 3 months

C. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.
   1. Additional off-label NCCN compendial uses for temozolomide, meeting NCCN categories 1, 2a or 2b, are approved for the following indications:
      a. Bone cancer- Ewing’s sarcoma family of tumors;
      b. Central nervous system (CNS) cancers:
         i. Adult intracranial and spinal ependymoma (excluding subependymoma);
         ii. Adult low-grade infiltrative supratentorial astrocytoma/oligodendroglioma (excluding pilocytic astrocytoma);
         iii. Adult medulloblastoma and supratentorial primitive neuroectodermal tumors (PNET);
         iv. Brain metastases, if Temodar was active against primary tumor;
         v. Primary CNS lymphoma;
      c. Lung neuroendocrine tumors (carcinoid);
      d. Melanoma;
      e. Neuroendocrine tumors:
         i. GI tract, lung, and thymus;
         ii. Neuroendocrine tumors of the pancreas;
         iii. Pheochromocytoma/paraganglioma;
      f. Non-Hodgkin’s lymphoma (NHL)- mycosis fungoides (MF)/Sezary syndrome (SS);
      g. Non-melanoma skin cancers- dermatofibrosarcoma protuberans (DFSP);
      h. Small cell lung cancer (SCLC);
      i. Soft tissue sarcoma:
         i. Angiosarcoma;
         ii. Retroperitoneal/intra-abdominal;
         iii. Rhabdomyosarcoma;
         iv. Solitary fibrous tumor/hemangiopericytoma;
         v. Extremity/superficial trunk, head/neck;
      j. Uterine neoplasms - uterine sarcoma.

II. Continued Approval
   A. Glioblastoma and Anaplastic Astrocytoma (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria.

      Approval duration: 6 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
      2. Refer to ERX.SPMN.16 - Global Biopharm Policy.
Background

Description/Mechanism of Action:
Temodar contains temozolomide, an imidazotetrazine derivative. Temozolomide is not directly active but undergoes rapid nonenzymatic conversion at physiologic pH to the reactive compound 5-(3-methyltriazen-1-yl)-imidazole-4-carboxamide (MTIC). The cytotoxicity of MTIC is thought to be primarily due to alkylation of DNA. Alkylation (methylation) occurs mainly at the O\textsuperscript{6} and N\textsuperscript{7} positions of guanine.

Formulations:
Capsule, oral:
- Temodar and generic: 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, 250 mg
Solution reconstituted, intravenous:
- Temodar: 100 mg (1 ea)

*The recommended dose for Temodar as an IV infusion over 90 minutes is the same as the dose for the oral capsule formulation; bioequivalence has been established only when Temodar for injection was given over 90 minutes.

FDA Approved Indications:
Temodar is an alkylating (methylating) drug/oral capsule and IV formulation indicated for:
- Newly diagnosed glioblastoma multiforme:
  - Treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment.
- Refractory anaplastic astrocytoma:
  - Treatment of adult patients with refractory anaplastic astrocytoma, i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

Appendices

Appendix A: Abbreviation Key
CNS: central nervous system  
DFSP: dermatofibrosarcoma protuberans  
GBM: glioblastoma multiforme  
MF: mycosis fungoides  
MGMT: methylguanine methyl-transferase  
MTIC: 5-(3-methyltriazen-1-yl)-imidazole-4-carboxamide  
NHL: non-Hodgkin’s lymphoma  
PNET: primitive neuroectodermal tumors  
SCLC: small cell lung cancer  
SS: Sezary syndrome  
WHO: World Health Organization

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.
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<th>Description</th>
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<td>J9328</td>
<td>Injection, temozolomide, 1 mg</td>
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<tr>
<td>J8700</td>
<td>Temozolomide, oral, 5 mg</td>
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### Reviews, Revisions, and Approvals

<table>
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<tr>
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<th>Approval Date</th>
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- **Policy created.**
- **Added efficacy and safety data for Temodar. Added Appendices A, B, C, D, E. Added figure 2 to allow for off-label and NCCN supported uses.**
- **Algorithm 1: added initial criteria for Temodar for GBM, PCP question, and approval period for 42 days; direction to figure 2 placed instead of denial to allow off-label use. References reviewed and updated as needed.**
- **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.**

### References

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.

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