I. Medication Description

Temozolomide is an oral chemotherapy agent that causes tumor cell death by preventing cell division and cell multiplication. It is not directly active, but undergoes rapid conversion at physiologic pH to a reactive compound (MTIC). The cytotoxicity of MTIC is thought to be primarily due to alkylation of DNA. Alkylation (methylation) occurs mainly at the O6 and N7 positions of guanine.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage for Temodar® is provided when prescribed by an oncologist in accord with the following:

- Adult Intracranial and Spinal Ependymoma as a single agent for disease progression
- Adult Meduloblastoma/Supratentorial Primitive Neuroectodermal Tumors (PNET) as a single agent for patients who have received prior chemotherapy
- Advanced Metastatic Melanoma
  - As a single agent for disease that is surgically incurable and unresectable AND
  - As second-line or subsequent therapy for disease progression AND
  - Patient’s performance status is 0-2
- Anaplastic Gliomas:
  - As adjunctive treatment with concurrent radiation OR
  - Recurrent disease or salvage therapy as a single agent or in combination with bevacizumab
- Astrocytoma/Oligodendroglioma: as a single agent for recurrent or progressive disease after radiation
- Ewing’s Sarcoma in combination with irinotecan with or without vincristine
  - For progressive disease following primary treatment OR
  - For relapsed disease with or without radiation OR
  - As second-line therapy for metastatic disease
- Glioblastoma:
  - Treatment of recurrent disease as a single agent or in combination with bevacizumab OR
  - Adjuvant treatment following resection:
    - With concurrent radiation therapy followed by temozolomide alone for patients with good performance status (KPS 60 or greater) OR
    - As a single agent if tumor is methylguanine methyltransferase positive for
- Patients over 70 years of age with good performance status (KPS 60 or greater) OR
- Patients with poor performance status (KPS less than 60)

- Lung Neuroendocrine Tumors: treatment of Stage IIIb to IV low to intermediate grade neuroendocrine carcinoma of the lung
- Metastatic Central Nervous System Lesions (brain metastases) where active against primary tumor:
  - Single agent treatment for recurrent disease OR
  - Single agent treatment for brain metastases with recurrent stable systemic disease
- Mycosis Fungoides/Sezary Syndrome: as second-line chemotherapy
- Neuroendocrine Tumors of the Pancreas: as a single-agent or in combination with capecitabine for the treatment of unresectable locoregional disease or distant metastases with:
  - Symptomatic disease OR
  - Clinically significant tumor burden OR
  - Clinically significant progression
- Nonmelanoma Skin Cancers
  - Dermatofibrosarcoma Protuberans (DFSP): for metastatic disease.
- Pheochromocytoma/Paraganglioma- single agent as a primary treatment for distant metastases
- Primary Central Nervous System Lymphoma:
  - As primary treatment with methotrexate and rituximab OR
  - Progressive or recurrent disease:
    - Single agent or in combination with rituximab for patients who have received a prior methotrexate regimen without prior radiation therapy OR
    - Single agent or in combination with rituximab for progression or recurrent disease in patients with prior whole brain radiation therapy OR
    - Single agent in combination with rituximab for progression or recurrent disease in patients who received prior high-dose chemotherapy with stem cell reserve after prolonged response
- Small Cell Lung Cancer:
  - Subsequent therapy as a single agent in patients with PS of 0-2
    - For recurrent or relapsed disease within 6 months of complete or partial response to initial therapy OR
    - For primary progressive disease
- Soft Tissue Sarcoma:
  - Located in retroperitoneal/intra-abdominal, head/neck, or extremity/trunk regions: Single-agent palliative chemotherapy for unresectable or progressive disease
  - For Solitary fibrous tumor/Hemangiopericytoma: In combination with bevacizumab
  - For angiosarcoma as a single agent for palliative therapy
  - For rhabdomyosarcoma
    - Single agent for pleomorphic disease for palliative therapy
    - In combination with vincristine and irinotecan for non-pleomorphic disease
- Uterine Sarcoma as a single agent
  - Medically inoperable disease limited to uterus OR
  - Following TH (with or without BSO)for stage II—IV disease OR
  - Recurrent and metastatic disease
IV. **Quantity Limitations**

Available for dosing as supported by FDA guidelines and Compendia.

V. **Coverage Duration**

- Astrocytoma/oligodendroglioma, anaplastic astrocytoma and glioblastoma multiforme: 12 months and may be renewed
- All other indications: 6 months and may be renewed

VI. **Coverage Renewal Criteria**

Coverage can be renewed based upon the following criteria:
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread **AND**
- Absence of unacceptable toxicity from the drug

VII. **Billing/Coding Information**

Available as 5mg, 20mg, 100mg, 140mg, 180mg, and 250mg capsules

VIII. **Summary of Policy Changes**

- 9/1/11: addition of the following diagnoses and criteria for coverage:
  - Primary central nervous system lymphoma
  - Ewing’s sarcoma
  - Metastatic central nervous system lesions (i.e., brain metastases)
  - Mycosis fungoides (MF)/Sezary syndrome (SS)
  - Soft tissue sarcoma
- 9/15/12: Clarification of treatment for astrocytoma and oligodendroglioma; addition of treatment for refractory glioblastoma multiforme; addition of ICD codes 171.4 and 171.6
- 9/15/13: Removal of specific dosing recommendations; Addition of covered indications: meduloblastoma, PNET, neuroendocrine tumors of pancrease, uterine sarcoma, SCLC, lung neuroendocrine tumor
- 9/15/14: updated coverage criteria to match current category 1 and 2A NCCN recommendations
- 7/1/15: formulary distinctions made
- 12/15/15: updated indications to include coverage in DFSP; criteria updated in accordance with current NCCN treatment recommendations
- 9/15/16: policy updated to correspond with current NCCN treatment guidelines

IX. **References**

1. UpToDate Online, retrieved April 2011
The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary agent will be considered. The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.