Clinical Policy Bulletin:
Temozolomide (Temodar)

Number: 0000

Policy

Aetna considers temozolomide (Temodar) injection medically necessary for members who are unable to take the oral formulation of temozolomide due to vomiting or inability to absorb capsules sufficiently through the gastrointestinal tract, for the following indications:

- Ewing's Sarcoma Family of Tumors – for progressive, relapsed or metastatic disease
- Adult Low-Grade Infiltrative Supratentorial Astrocytoma/Oligodendroglioma (excluding pilocytic astrocytoma) – adjuvant chemotherapy, or for recurrent or progressive disease
- Adult Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumors (PNET) – progression or recurrence (salvage therapy)
- Anaplastic Gliomas – adjuvant treatment, and treatment of recurrent disease or salvage therapy
- Glioblastoma – treatment following resection, or for recurrent disease or salvage therapy
- Central Nervous System Cancers - Limited (1-3) Metastatic Lesions – for brain metastases in disseminated or recurrent disease
- Central Nervous System Cancers - Multiple (>3) Metastatic Lesions – for brain metastases in recurrent stable systemic disease
- Primary CNS Lymphoma – primary treatment or for progressive or recurrent disease
- Lung Neuroendocrine Tumors- treatment of stage IIIb-IV low- or intermediate-grade neuroendocrine carcinoma
- Melanoma - unresectable, recurrent or metastatic disease
- Carcinoid Tumors - unresectable or metastatic progressive disease
- Neuroendocrine Tumors of the Pancreas (Islet Cell Tumors) – unresectable locoregional disease or distant metastatic disease
- Mycosis Fungoides (MF)/Sezary Syndrome (SS) – second line chemotherapy
- Small cell lung cancer – primary progressive disease or relapse
Angiosarcoma
Soft tissue sarcoma of the extremity/trunk - synchronous stage IV or recurrent disease with disseminated metastases
Retroperitoneal/intraabdominal soft tissue sarcoma – unresectable or progressive disease
Solitary Fibrous Tumor/Hemangiopericytoma
Uterine sarcoma

Aetna considers temozolomide experimental and investigational for all other indications.

Background

Temodar (temozolomide) was approved by the U.S. Food and Drug Administration for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment. The labeling states that temozolomide is indicated for the treatment of adult patients with refractory anaplastic astrocytoma (i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine).

Guidelines from the National Comprehensive Cancer Network (2013) list the following indications for temozolomide:

- Ewing's Sarcoma Family of Tumors - used with growth factor support in combination with irinotecan with or without vincristine
  with or without radiation therapy for relapse
  for progressive disease following primary treatment
  as second-line therapy for metastatic disease
- Adult Low-Grade Infiltrative Supratentorial Astrocytoma/Oligodendroglioma (excluding pilocytic astrocytoma)
  Treatment as a single agent for recurrent or progressive disease
  Adjuvant chemotherapy as a single agent following maximal safe resection biopsy or subtotal resection
- Adult Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumors (PNET) - recurrence/salvage therapy as a single agent for disease progression in patients who have received prior chemotherapy
- Anaplastic Gliomas
  Adjuvant treatment as concurrent chemoradiation for anaplastic oligodendroglioma, anaplastic oligoastrocytoma, and anaplastic astrocytoma single-agent chemotherapy
  Treatment of recurrent disease or salvage therapy as a single agent or in combination with bevacizumab
- Glioblastoma
  Treatment following resection with or without carmustine polymer as concurrent and adjuvant treatment in combination with radiation therapy (RT) for patients with good performance status (PS; Karnofsky Performance Status [KPS] ≥70 )
chemotherapy for patients age >70 years with good PS if methylguanine methyltransferase promotor-methylation positive
chemotherapy for patients with poor PS (KPS <70)
Treatment of recurrent disease or salvage therapy as a single agent or in combination with bevacizumab

Central Nervous System Cancers - Limited (1-3) Metastatic Lesions - consider as a single-agent treatment for brain metastases if active against the primary tumor
as primary treatment for disseminated disease with poor systemic treatment options for recurrent disease

Central Nervous System Cancers - Multiple (>3) Metastatic Lesions - Single-agent treatment if active against primary tumor for brain metastases in persons with recurrent stable systemic disease

Primary CNS Lymphoma
Primary treatment combined with high-dose methotrexate and rituximab with deferred radiation therapy
Treatment as a single agent or in combination with rituximab for progressive disease in patients who have received prior methotrexate-based regimen without prior radiation therapy (RT) after prolonged response to prior regimen in combination with RT after short or no response to prior regimen
Consider systemic treatment as a single agent or in combination with rituximab for progressive or recurrent disease in patients with prior who brain radiation therapy

Lung Neuroendocrine Tumors
Use as treatment for stage IIIb (T4 due to multiple lung nodules)-IV low- or intermediate-grade neuroendocrine carcinoma

Melanoma
Single agent or in combination with cisplatin and vinblastine with or without interleukin-2 and interferon alfa for unresectable stage III in-transit metastases local/satellite and/or intransit unresectable recurrence incompletely resected or unresectable nodal recurrence recurrent or metastatic disease in patients with good performance status

Carcinoid Tumors - Management of clinically significant locoregional unresectable or metastatic progressive disease Neuroendocrine Tumors of the Pancreas (Islet Cell Tumors) - Management of unresectable locoregional disease and/or distant metastatic disease in patients with symptoms, clinically significant tumor burden, or clinically significant progression

Mycosis Fungoides (MF)/Sezary Syndrome (SS)
Second-line chemotherapy for patients with Small Cell Lung Cancer (SCLC)
stage IA-IIA MF with histologic evidence of folliculotropic or large cell transformation or stage IIB with generalized extent
tumor, transformed, and/or folliculotropic disease in combination with skin-directed therapy stage IV non-Sezary or visceral disease refractory or progressive stage III MF or SS

Small cell lung cancer
Subsequent chemotherapy for patients with performance status 0-2 as a single agent for relapse within 6 months following complete or partial response with initial treatment primary progressive disease

Angiosarcoma - Used as a single agent for angiosarcoma
Soft Tissue Sarcoma of the Extremity/Trunk - Single-agent palliative chemotherapy for synchronous stage IV or recurrent disease with disseminated metastases
Retroperitoneal/Intraabdominal Soft Tissue Sarcoma - Single-agent palliative chemotherapy for unresectable or progressive disease
Rhabdomyosarcoma - Therapy for pleomorphic rhabdomyosarcoma as a single agent nonpleomorphic rhabdomyosarcoma in combination with vincristine and irinotecan

Solitary Fibrous Tumor/Hemangiopericytoma - In combination with bevacizumab for the treatment of solitary fibrous tumor and hemangiopericytoma
Uterine Sarcoma - Single agent for medically inoperable disease limited to the uterus may be considered following total hysterectomy with bilateral salpingo-oophorectomy (TH/BSO) for stage I-III disease following TH/BSO for stage IV disease for local recurrence confined to the vagina for extrapelvic recurrence with no prior radiation therapy for isolated metastases. Consider postoperative chemotherapy for resectable isolated metastases for disseminated metastases

Nausea and vomiting are known side effects of treatment and should be medically treated, when they occur. Current dosing recommendations by the manufacturer are not to withhold doses due to the adverse effects of vomiting. Grade 3 or 4 vomiting occurred < 1% in the clinical trials.

The above policy is based on the following references:
