VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Temozolomide Intravenous Utilization Management Medical Policy
- Temodar® (temozolomide intravenous infusion – Merck, generic)

REVIEW DATE: 10/11/2023

OVERVIEW

Temozolomide, an alkylating agent, is indicated in adults for the following uses:[1]

- **Anaplastic astrocytoma**,
  - Newly diagnosed as adjuvant treatment
  - Refractory
- **Glioblastoma**, newly diagnosed, concomitantly used with radiotherapy and then as maintenance therapy.

Dosing Information

A pharmacokinetic study established bioequivalence between temozolomide 150 mg/m^2 administered as a 90 minute intravenous infusion and temozolomide 150 mg/m^2 oral administration of the capsule formulation.[1] The dose of temozolomide should be adjusted based on the nadir neutrophil and platelet counts, and the neutrophil and platelet counts prior to initiating the next cycle of therapy. Dosing information for the indications listed in FDA-Approved Indications and Other Uses with Supportive Evidence is supported by the prescribing information and various clinical studies.[1, 3-54]

Guidelines

The National Comprehensive Cancer Network (NCCN) Compendium recommends use of temozolomide for the indications listed in the FDA-Approved Indications and Other Uses with Supportive Evidence sections.[2]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of temozolomide. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with temozolomide as well as the monitoring required for adverse events and long-term efficacy, approval requires temozolomide to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of temozolomide intravenous is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Anaplastic Astrocytoma.** Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 200 mg/m^2 administered intravenously daily for up to 5 days of each 28-day cycle.

2. **Glioblastoma Multiforme.** Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist.
   Note: This includes glioblastoma and grade IV astrocytoma.

   Dosing. Approve one of the following dosing regimens (A or B):
   A) Initial (Concomitant) Phase: Administer up to 75 mg/m^2 intravenously daily for up to 49 days; OR
   B) Maintenance Phase: Administer up to 200 mg/m^2 intravenously daily for up to 5 days of each 28-day cycle.

Other Uses with Supportive Evidence

3. **Bone Cancer.** Approve for 1 year if the patient meets the following (A, B, and C):
   A) Patient has tried one chemotherapy regimen; AND
   Note: Examples of a chemotherapy regimen include one or more of the following products: vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide.
   B) Patient has ONE of the following diagnosis (i or ii):
   i. Ewing sarcoma; OR
   ii. Mesenchymal chondrosarcoma; AND
   C) Temozolomide is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 150 mg/m^2 administered intravenously for up to 5 days of each 21-day cycle.

4. **Brain Metastases from Solid Tumors.** Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist.

   Dosing. Approve one of the following dosing regimens (A, B, or C):
   A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days of each 28-day cycle; OR
   B) Administer up to 150 mg/m^2 intravenously daily for up to 14 days of each 28-day cycle; OR
   C) Administer up to 75 mg/m^2 intravenously daily for up to 42 days of each 56-day cycle.

5. **Ependymoma, Intracranial or Spinal.** Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 200 mg/m^2 administered intravenously daily for up to 5 days of each 28-day cycle.

6. **Glioma, Other Types.** Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist:

Note: Examples of other types of gliomas include pediatric diffuse high-grade glioma, oligodendroglioma, low-grade glioma, and circumscribed glioma. For anaplastic astrocytoma and glioblastoma multiforme, refer to the respective criteria under the FDA-approved indications.

Dosing. Approve one of the following dosing regimens (A, B, C, or D):
A) Administer up to 75 mg/m^2 intravenously daily for up to 49 days of each 77-day cycle; OR
B) Administer up to 75 mg/m^2 intravenously daily for up to 21 days of each 28-day cycle; OR
C) Administer up to 200 mg/m^2 intravenously daily for up to 5 days in each 28-day cycle; OR
D) Administer up to 150 mg/m^2 intravenously daily for up to 14 days of each 28-day cycle.

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7. Gliosarcoma. Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist.
Dosing. Approve one of the following dosing regimens (A or B):
A) Initial (Concomitant) Phase: Administer up to 75 mg/m^2 intravenously daily for up to 49 days; OR
B) Maintenance Phase: Administer up to 200 mg/m^2 intravenously daily for up to 5 days of each 28-day cycle.

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8. Medulloblastoma. Approve for 1 year if the patient meets the following (A and B):
A) Patient has tried one chemotherapy; AND
Note: Examples of a chemotherapy regimen include one or more of the following products: cisplatin, cyclophosphamide, vincristine, lomustine.
B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Administer up to 200 mg/m^2 intravenously daily for up to 5 days in each 21-day or 28-day cycle.

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9. Melanoma. Approve for 1 year if the patient meets the following (A, B, and C):
A) Patient has unresectable or metastatic disease; AND
B) Patient has tried one systemic regimen; AND
Note: Examples of a systemic regimen include one or more of the following medications: Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Yervoy (ipilimumab intravenous infusion), Tafinlar (dabrafenib capsule), Mekinist (trametinib tablet), Zelboraf (vemurafenib tablet), Cotellic (cobimetinib tablet), Braftovi (encorafenib capsule), Mektovi (binimetinib tablet).
C) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):
A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days in each 28-day cycle; OR
B) Administer up to 75 mg/m^2 intravenously daily for up to 42 days of each 56-day cycle; OR
C) Administer up to 75 mg/m^2 intravenously daily for up to 21 days of each 28-day cycle.

Mycosis Fungoides/Sézary Syndrome. Approve for 1 year if the patient meets the following (A, B, and C):

A) Patient has tried one prior therapy; AND
Note: Examples of a prior therapy include topical carmustine, topical corticosteroids, topical imiquimod, topical retinoids, Adcetris (brentuximab vedotin intravenous infusion), gemcitabine.
B) Patient has central nervous system (CNS) involvement; AND
C) Temozolomide is prescribed by or in consultation with an oncologist or dermatologist.

Dosing. Approve up to 200 mg/m^2 administered intravenously daily for up to 5 days in each 28-day cycle.

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10. Neuroendocrine Tumors. Approve for 1 year if the patient meets one of the following (A and B):
A) Patient has ONE of the following diagnosis (i, ii, iii, iv, v, or vi):
i. Carcinoid tumors or neuroendocrine tumor of the gastrointestinal tract, lung, or thymus; OR
ii. Islet cell tumors or pancreatic neuroendocrine tumors; OR
iii. Extrapulmonary poorly differentiated neuroendocrine carcinoma; OR
iv. Patient has large or small cell carcinoma; OR
v. Patient has mixed neuroendocrine–non-neuroendocrine neoplasm; OR
vi. Well differentiated grade 3 neuroendocrine tumor; AND
B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):
A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days in each 28-day cycle; OR
B) Administer up to 150 mg/m^2 intravenously daily for up to 14 days of each 28-day cycle.

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11. Pheochromocytoma or Paragangliomas. Approve for 1 year if the patient meets the following (A and B):
A) Patient has unresectable or metastatic disease; AND
B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):
A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days in each 28-day cycle; OR
B) Administer up to 150 mg/m^2 intravenously daily for up to 14 days of each 28-day cycle.

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12. Primary Central Nervous System Lymphoma. Approve for 1 year if temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 200 mg/m^2 administered intravenously daily for up to 5 days in each 21-day or 28-day cycle.

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13. Small Cell Lung Cancer. Approve for 1 year if the patient meets the following (A and B):
A) Patient has tried one systemic regimen; AND
Note: Examples of systemic regimen include one or more of the following products: cisplatin, etoposide, carboplatin, Tecentriq (atezolizumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), irinotecan.

B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):
A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days in each 28-day cycle; OR
B) Administer up to 75 mg/m^2 intravenously daily for up to 21 days of each 28-day cycle.

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14. Soft Tissue Sarcoma. Approve for 1 year if the patient meets the following (A and B):
A) Patient meets one of the following (i or ii):
i. Patient has advanced or metastatic disease OR
ii. Patient has ONE of the following diagnoses (a or b):
a) Non-pleomorphic rhabdomyosarcoma; OR
b) Solitary fibrous tumor; AND
B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, C, or D):
A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days of each 21-day or 28-day cycle; OR
B) Administer up to 100 mg/m^2 intravenously daily for up to 21 days of each 28-day cycle; OR
C) Administer up to 100 mg/m^2 intravenously daily for up to 42 days of each 63-day cycle; OR
D) Approve up to 150 mg/m^2 administered intravenously daily for up to 14 days of each 28-day cycle.

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15. Uterine Sarcoma. Approve for 1 year if the patient meets the following (A and B):
A) Patient has tried a chemotherapy regimen; AND
Note: Examples of a chemotherapy regimen include one or more of the following products: doxorubicin, docetaxel, epirubicin, gemcitabine, ifosfamine, dacarbazine, vinorelbine.
B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A, B, or C):
A) Administer up to 200 mg/m^2 intravenously daily for up to 5 days of each 28-day cycle; OR
B) Administer up to 100 mg/m^2 intravenously daily for up to 21 days of each 28-day cycle; OR
C) Administer up to 100 mg/m^2 intravenously daily for up to 42 days of each 63-day cycle.

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16. Uveal Melanoma. Approve for 1 year if the patient meets the following (A and B):
A) Patient has unresectable or metastatic disease; AND
B) Temozolomide is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):
A) Administer up to 75 mg/m^2 intravenously daily for up to 21 days of each 28-day cycle; OR
B) Administer up to 150 mg/m^2 intravenously daily for up to 14 days of each 28-day cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of temozolomide is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Anaplastic Gliomas:** This condition of approval and dosing were removed.	09/14/2022

	Glioma, Other Types: The condition of approval of "low-grade glioma" was renamed to "glioma, other types." The requirement that the patient has World Health Organization (WHO) Grade I or II glioma was removed. A note was added with types of glioma and to refer to the respective criteria under the FDA-approved indications for anaplastic astrocytoma and glioblastoma multiforme. The dosing of administer up to 150 mg/m^2 intravenously daily for up to 14 days of each 28-day cycle was added as an option. **Melanoma:** The requirement of trial of systemic regimen was added. A note was added with examples of a systemic regimen. **Neuroendocrine Tumors**: The words "extrapulmonary" and "neuroendocrine carcinoma" were added to the condition "poorly differentiated." The condition "large or small cell (other than lung)" was reworded to "large or small cell carcinoma." The following condition was added: mixed neuroendocrine-non-neuroendocrine neoplasm. **Soft Tissue Sarcoma:** For the criteria from patients with advanced, unresectable, or metastatic disease, angiosarcoma was removed and pleomorphic rhabdomyosarcoma was added.	
Annual Revision	The overview section was updated to include the new labeled indication of "newly diagnosed anaplastic astrocytoma as adjuvant treatment." The refractory anaplastic astrocytoma was updated to remove the following wording, "in patients who have experienced disease progression on a drug regimen containing nitrosourea (i.e., BiCNU® [carmustine {BCNU} intravenous infusion] or lomustine [CCNU] capsules) and Matulane® (procarbazine capsules)." For all the indications, the duration of approval was updated from 6 months to 1 year. **Glioma, Other Types**: The note was updated to state "examples of glioma" and circumscribed glioma was added. **Pheochromocytoma or Paragangliomas**: The criterion which states "patient has metastatic disease" was updated to state "patient has unresectable or metastatic disease." **Primary Cutaneous Anaplastic Large Cell Lymphoma:** This condition for approval and dosing was removed. **Soft Tissue Sarcoma:** The criteria which states "patient has advanced, unresectable, or metastatic disease and one of the following diagnoses: pleomorphic rhabdomyosarcoma or soft tissue sarcoma with unknown histology" was updated to state "patient has advanced or metastatic disease." **Uveal Melanoma:** The criterion which states that patient has metastatic disease was updated to state "patient has unresectable or metastatic disease."	10/11/2023