Temozolomide for Injection

NDC CODE(S) 00085-1381-XX TEMODAR 100MG Solution Reconstituted (MERCK SHARP & DOHME)

DESCRIPTION

Temozolomide is a cytotoxic agent of the imidazotetrazine class. It is a second generation alkylating agent and a methylating agent. While chemically related to another methylating agent, dacarbazine (DTIC), unlike DTIC, it does not require hepatic metabolism for activation. Administered orally or by injection, temozolomide is spontaneously hydrolyzed to its active state with rapid, near-100% bioavailability. Temozolomide enters the spinal fluid and its cytotoxicity is thought to be primarily due to alkylation of DNA but, as with other methylating agents (i.e., procarbazine, streptozotocin and DTIC), it forms no DNA crosslinks. Temozolomide has activity against a variety of solid tumors and demonstrates minimal, non-cumulative myelosuppression that is rapidly reversible.

POLICY

- Temozolomide is considered ***medically necessary*** for the treatment of the following if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Bone Cancer
  - Central Nervous System (CNS) Cancer
  - Primary CNS Lymphoma
  - Melanoma, cutaneous
  - Melanoma, uveal
  - Mycosis fungoides/Sézary syndrome
  - Neuroendocrine Tumors
  - Primary cutaneous CD30+ T-cell lymphoproliferative disorders
  - Small Cell Lung Cancer
  - Soft Tissue Sarcoma
  - Uterine Sarcoma
- Temozolomide for the treatment of other conditions/diseases is considered ***investigational***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Temozolomide is considered **medically appropriate** for **ANY ONE** of the following diagnoses:
  - Bone Cancer if **ALL** of the following:
    - Documented diagnosis of Ewing's Sarcoma
    - Used in combination with irinotecan for **ANY ONE** of the following:
      - Progressive disease following primary treatment
      - Second line therapy for metastatic disease
      - Used for relapsed disease
  - Central Nervous System (CNS) Cancer further classified as **ANY ONE** of the following:
    - Glioblastoma multiforme (GBM) if **ANY ONE** of the following:
      - Used concomitantly with radiotherapy and then as a single agent as maintenance treatment for newly diagnosed disease
      - Used as adjuvant treatment as a single agent and **ANY ONE** of the following:
        - Used concurrently or following radiotherapy

- Used as chemotherapy for individuals with O6-methylguanine-DNA methyltransferase (MGMT) promoter methylated tumors
- Individual has recurrent disease and **ANY ONE** of the following:
  - Used as a single agent
  - Used in combination with bevacizumab
- Astrocytoma/Oligodendroglioma-Low-grade (WHO Grade II) Infiltrative, Supratentorial and **ANY ONE** of the following:
  - Used as adjuvant treatment as a single agent either concurrently or following radiation therapy and individual has high risk features (i.e., > 40 years of age, subtotal resection or biopsy, tumor size, neurologic deficits, presence of sequencing verified IDH wild type)
  - Used for recurrent or progressive disease as a single agent either concurrently or following radiation therapy
- Adult Intracranial and Spinal Ependymoma if **ALL** of the following:
  - Used as a single agent for progression or recurrent disease
  - Individual is refractory to surgery or prior radiation therapy
  - Individual does **NOT** have subependymoma
- Adult medulloblastoma used as a single agent for disease reoccurrence in individuals who received prior chemotherapy
- Anaplastic Gliomas (Anaplastic Astrocytoma, Anaplastic Oligoastrocytoma, Anaplastic oligodendroglioma–1p19p codeleted) if **ANY ONE** of the following:
  - Individual has recurrent disease and used as a single agent or in combination with bevacizumab
  - Used for individuals with KPS ≥60 (i.e., ECOG 0-2) as adjuvant treatment as a single agent either concurrently or following standard radiation therapy
  - Individual has refractory Anaplastic Astrocytoma and used as a single agent for disease progression on a nitrosourea and procarbazine containing regimen
- CNS Metastases as a single agent therapy for **ANY ONE** of the following:
  - Used as initial treatment in individuals with small asymptomatic brain metastases
  - Used for relapsed disease in individuals with limited brain metastases and stable systemic disease or reasonable treatment options
  - Individual has recurrent limited brain metastases
  - Used for recurrent disease in individuals with extensive brain metastases and stable systemic disease or reasonable systemic treatment options

- Primary CNS Lymphoma if **ANY ONE** of the following:
  - Used in combination with rituximab and high-dose methotrexate if **ANY ONE** of the following:
    - Used as induction therapy
    - Used as consolidation therapy in individuals who have had a complete response or complete response unconfirmed (Cru) to induction therapy
  - Used as a single agent or in combination with rituximab for individuals with relapsed or refractory disease
- Melanoma, cutaneous if **ALL** of the following:
  - Used as a single agent therapy
  - Individual has unresectable or metastatic disease
  - Used as subsequent therapy in individuals who have had disease progression (or maximum clinical benefit achieved) from BRAF targeted therapies (i.e., dabrafenib, trametinib, vemurafenib)
- Melanoma, uveal used as single agent for distant metastatic disease
- Neuroendocrine Tumors (NET) if **ANY ONE** of the following:
  - Documented pancreatic neuroendocrine tumors if **ALL** of the following:
    - Used in combination with capecitabine
    - Disease is locally advanced or metastatic

- Individual has symptomatic or bulky (i.e., or clinically significant tumor burden) or progressive disease
- Documented Pheochromocytoma/Paraganglioma used as primary treatment for distant metastases in combination with octreotide or lanreotide
- Individual has disease in the lung/thymus with carcinoid syndrome that is poorly controlled and **ALL** of the following:
  - Used as a single agent or in combination with capecitabine
  - Used in combination with octreotide LAR, lanreotide or telotristat for persistent symptoms (e.g. diarrhea, etc.)
- Individual has bronchopulmonary or thymic disease and **ALL** of the following:
  - Will **NOT** be used for adjuvant therapy
  - Used as a single agent or in combination with capecitabine for **ANY ONE** of the following:
    - Individual has distant metastatic disease with clinically significant tumor burden and low grade (typical) histology, evidence of progression, intermediate grade (atypical) histology or symptomatic disease
    - Individual has locally advanced unresectable disease
- Individual has Poorly Differentiated (i.e., high grade) Neuroendocrine Carcinoma or Large or Small Cell Carcinoma (other than lung) as a single agent or in combination with capecitabine for **ANY ONE** of the following:
  - Used for locally advanced unresectable or metastatic disease
  - Used as neoadjuvant or adjuvant therapy or as chemotherapy alone for resectable disease

- Mycosis fungoides/Sézary syndrome and **ALL** of the following:
  - Individual has CNS involvement
  - Individual does **not** have relapsed or persistent stage IA-IIA mycosis fungoides with B1 blood involvement
- Primary cutaneous CD30+ T-cell lymphoproliferative disorders for **ALL** of the following:
  - Individual has primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions or cutaneous ALCL with regional nodes (excludes systemic ALCL)
  - Used as a single agent for relapsed or refractory disease with CNS involvement
- Small Cell Lung Cancer and used as subsequent therapy as a single agent for **ANY ONE** of the following:
  - Individual has relapsed disease within 6 months following initial treatment
  - Individual has primary progressive disease
- Soft Tissue Sarcoma and **ANY ONE** of the following:
  - Used as palliative therapy as a single agent for **ANY ONE** of the following:
    - Individual has angiosarcoma
    - Individual has retroperitoneal or intra-abdominal disease used as subsequent therapy for recurrent unresectable or stage IV disease
    - Individual has pleomorphic rhabdomyosarcoma and used as subsequent therapy for advanced or metastatic disease
    - Individual has sarcoma of the extremity/body wall or head/neck and used as subsequent therapy for advanced or metastatic disease
    - Individual has solitary fibrous tumor
    - Individual has undifferentiated pleomorphic sarcoma (UPS)
  - Used in combination with vincristine and irinotecan for non-pleomorphic rhabdomyosarcoma
  - Used in combination with bevacizumab for solitary fibrous tumor
- Uterine Sarcoma and used as a single agent for recurrent or metastatic disease which has progressed following prior cytotoxic chemotherapy

RENEWAL CRITERIA

- Temozolomide is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Disease Response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread
  - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: myelosuppression (pancytopenia, leukopenia, anemia), myelodysplastic syndrome or secondary malignancy, pneumocystis pneumonia, severe hepatotoxicity, etc.

INDICATION(S)	DOSAGE & ADMINISTRATION
All indications	Up to 200mg/m² intravenously on days 1 thru 5 of a 28 day cycle

LENGTH OF AUTHORIZATION

Coverage is provided for 6 months and may be renewed.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Lexi-Comp Online. (2020, March). AHFS DI. *Temozolomide*. Retrieved November 19, 2020 from Lexi-Comp Online with AHFS.

MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2020, June). *Temozolomide*. Retrieved November 19, 2020 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium®. *Temozolomide.* Retrieved November 19, 2020 from the National Comprehensive Cancer Network.

U. S. Food and Drug Administration. (2019, November). Center for Drug Evaluation and Research. Product Information. *Temodar® (temozolomide).* Retrieved November 23, 2020 from http://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022277s011lbl.pdf.

EFFECTIVE DATE 4/2/21

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