Medical Policy
Tumor Treatment Fields Therapy for Glioblastoma

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Policy Number: 514
BCBSA Reference Number: 1.01.29
NCD/LCD: Local Coverage Determination (LCD): Tumor Treatment Field Therapy (TTFT) (L34823)

Related Policies
- Analysis of MGMT Promoter Methylation in Malignant Gliomas, #587
- Intensity-Modulated Radiotherapy: Central Nervous System Tumors, #910
- Intracavitary Balloon Catheter Brain Brachytherapy for Malignant Gliomas or Metastasis to the Brain, #602
- Intraoperative Radiotherapy, #278
- Stereotactic Radiosurgery and Stereotactic Body Radiotherapy, #277

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Tumor treating fields therapy to treat glioblastoma is considered INVESTIGATIONAL, including but not limited to the following situations:
- As an alternative to standard chemotherapy for patients with progressive or recurrent glioblastoma multiforme after initial or repeat treatment with surgery, radiotherapy, and/or chemotherapy.
- As an adjunct to standard maintenance therapy in patients with newly diagnosed glioblastoma multiforme following initial treatment with surgery, radiotherapy, and/or chemotherapy.

Medicare HMO BlueSM and Medicare PPO BlueSM Members

This is not a covered service.

Local Coverage Determination (LCD): Tumor Treatment Field Therapy (TTFT) (L34823)

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.
Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Commercial Managed Care (HMO and POS)</th>
<th>This is not a covered service.</th>
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<tr>
<td>Commercial PPO and Indemnity</td>
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<td>Medicare HMO BlueSM</td>
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<td>Medicare PPO BlueSM</td>
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CPT Codes / HCPCS Codes / ICD Codes
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes
There is no specific CPT code for this service.

HCPCS Codes

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<tr>
<th>HCPCS codes:</th>
<th>Code Description</th>
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<tr>
<td>E0766</td>
<td>Electrical stimulation device used for cancer treatment, includes all accessories, any type</td>
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Description
GLIOBLASTOME MULTIFORME
Glioblastomas, also known as glioblastoma multiforme (GBM), are the most common form of malignant primary brain tumor in adults. They comprise approximately 15% of all brain and central nervous system tumors and more than 50% of all tumors that arise from glial cells.¹ The peak incidence for GBM occurs between the ages of 45 and 70 years. GBMs are grade IV astrocytomas, the most deadly type of glial cell tumor, and are often resistant to standard chemotherapy.¹ According to the National Comprehensive Cancer Network, GBM is the “most lethal brain tumor with only a third of patients surviving for 1 year and less than 5% living beyond 5 years.”²

Treatment
The primary treatment for patients newly diagnosed with GBM is to resect the tumor, confirm a diagnosis while debulking the tumor to relieve symptoms of increased intracranial pressure or compression. At the time of surgery, some patients may undergo implantation of the tumor cavity with a carmustine (bischloroethylnitrosourea)-impregnated wafer.² The cure rate with local treatment is very low; therefore, postsurgical treatment involves adjuvant radiotherapy, chemotherapy (typically temozolomide), or a combination of the 2 therapies. After adjuvant therapy, some patients may undergo maintenance therapy with temozolomide. Prognostic factors for success of therapy are age, histology, and performance status or physical condition of the patient.

No standard treatment exists for recurrent GBM. In patients with disease that recurs after initial treatment, additional debulking surgery may be used if recurrence is localized. Other treatment options for recurrent disease include various forms of systemic medications such as bevacizumab, bevacizumab plus

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No standard treatment exists for recurrent GBM. In patients with disease that recurs after initial treatment, additional debulking surgery may be used if recurrence is localized. Other treatment options for recurrent disease include various forms of systemic medications such as bevacizumab, bevacizumab plus
chemotherapy (eg, irinotecan, bis-chloroethylnitrosourea/chloroethylnitrosourea, temozolomide), temozolomide, nitrosourea, procarbazine plus chloroethyl nitrosourea and vincristine), cyclophosphamide, and platinum-based agents.\textsuperscript{2}

Fractionated external-beam radiotherapy after surgery is standard adjuvant therapy and may be used to treat recurrent GBM. Response rates in recurrent disease are less than 10\%, and progression-free survival rates at 6 months are less than 20\%.\textsuperscript{2,3}

Testing for O6-methylguanine-DNA methyltransferase (MGMT) gene promoter methylation has been proposed as a method to predict which patients with malignant gliomas may benefit from alkylating agent chemotherapy (eg, temozolomide). Data from randomized controlled trials have shown that MGMT promoter methylation is a predictor to responding to alkylating chemotherapeutic agents. The response and overall survival rates with temozolomide are higher in patients who have MGMT promoter methylation. (See policy \#587 on Analysis of MGMT promoter methylation in malignant gliomas.)

**Tumor Treatment Fields Therapy**

Tumor treatment fields (TTF) therapy is a noninvasive technology intended to treat GBM on an outpatient basis using electrical fields.\textsuperscript{3-5} TTF therapy exposes cancer cells to alternating electric fields of low intensity and intermediate frequency, which are purported selectively both to inhibit tumor growth and reduce tumor angiogenesis. TTF are proposed to inhibit rapidly dividing tumor cells by 2 mechanisms: arrest of cell proliferation and destruction of cells while undergoing division.\textsuperscript{4,5}

Optune, formerly NovoTTF-100A System, is the only legally marketed TTF delivery system available in the United States. Optune is a portable battery or power supply operated device that produces alternating electrical fields within the human body. These fields are called tumor treatment fields and are applied to the patient’s shaved head using electrically insulated surface transducer arrays, such that resistively coupled electric currents are not delivered to the patient. The device is used at home on a continuous basis (20-24 hours a day for the duration of treatment). Patients can carry the device in a backpack or shoulder pack while carrying out activities of daily living.\textsuperscript{6}

**Summary**

Glioblastoma multiforme (GBM) is the most common and deadly malignant brain tumor. It has a very poor prognosis and is associated with low quality of life during of treatment. Tumor treatment fields (TTF) therapy is a new, noninvasive technology intended to treat glioblastoma using alternating electric fields.

For individuals who have progressive or recurrent GBM after initial or repeat surgery, radiotherapy, and/or chemotherapy—who receive TTF therapy as an alternative to standard chemotherapy, the evidence includes a randomized controlled trial (RCT) and nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. The published RCT reported no differences in outcomes between patients treated with TTF and with standard chemotherapy. This trial had several methodologic limitations. Comparisons made only included an active control of questionable efficacy, which might not reflect current standard of care. There was high dropout rate (>20\% of patients in each group were lost to follow-up) and, for the quality of life outcomes, approximately 25\% of enrolled patients had complete data. The 2 nonrandomized studies were small and had limited validity due to differences in the patient populations treated with TTF and standard care. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have newly diagnosed GBM on maintenance therapy after initial treatment with surgery, radiotherapy, and/or chemotherapy who receive TTF therapy as an adjunct to standard maintenance therapy, the evidence includes an RCT. Relevant outcomes include overall survival, disease-specific survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity.

The single RCT reported that patients who received TTF treatment plus temozolomide had longer progression-free survival (3.1 months) and overall survival (4.9 months) than patients who received temozolomide alone. The trial had methodologic limitations, including a lack of a placebo control,
differential dropout between groups, and the possibility of adherence bias for outcomes reported with per-protocol analysis. Further corroboration of these results is needed in high-quality RCTs. The evidence is insufficient to determine the effects of the technology on health outcomes.

### Policy History

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<th>Date</th>
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<tr>
<td>9/2017</td>
<td>BCBSA National medical policy review. Policy statements rewritten for clarity but tumor treating fields remains investigational for all indications. 9/1/2017.</td>
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<td>10/2016</td>
<td>BCBSA National medical policy review. Policy statements rewritten for clarity but tumor treating fields remains investigational for all indications. 10/1/2016.</td>
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<td>11/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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<td>5/2015</td>
<td>Local Coverage Determination (LCD): Tumor Treatment Field Therapy (TTFT) (L34730) added. Coding information clarified.</td>
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<td>10/2014</td>
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### Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

### References


