Tumor-Treatment Fields Therapy for Glioblastoma

Description of Procedure or Service

Glioblastoma multiforme is the most common and deadly malignant brain tumor. It has a very poor prognosis and is associated with low quality of life during the course of treatment. Tumor-treatment fields therapy is a new, noninvasive technology that is intended to treat glioblastoma using electrical fields.

Background

Glioblastomas, also known as glioblastoma multiforme (GBM), are the most common form of malignant primary brain tumor in adults, and they comprise approximately 15% of all brain and central nervous system tumors and more than 50% of all tumors that arise from glial cells. 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. According to the National Comprehensive Cancer Network (NCCN), GBM is the "deadliest brain tumor with only a third of patients surviving for one year and less than 5% living beyond 5 years."

The primary treatment for GBM is debulking surgery to remove as much of the tumor as possible. At that time, some patients may undergo implantation of the tumor cavity with a carmustine (BCNU) -impregnated wafer. Depending on the patient’s physical condition, adjuvant radiation therapy, chemotherapy (typically temozolomide), or a combination of the two are sometimes given. After adjuvant therapy, some patients may undergo maintenance therapy with temozolomide. No standard treatment exists for recurrent GBM. In patients with disease that recurs after these initial therapies, 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 (e.g., irinotecan, BCNU/CCNU, temozolomide), temozolomide, nitrosourea, PCV (procarbazine, CCNU, and vincristine), cyclophosphamide, and platinum-based agents. External beam radiotherapy also 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%.

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

The NovoTTF-100A™ System (Novocure Ltd., Haifa, Israel) has been approved by the U.S. Food and Drug Administration (FDA) to deliver TTF therapy. TTF therapy via the NovoTTF-
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100A™ System is delivered by a battery-powered, portable device that generates the fields via disposable electrodes that are noninvasively attached to the patient’s shaved scalp over the site of the tumor. The device is used by the patient at home on a continuous basis (20–24 hours per day) for the duration of treatment, which can last for several months. Patients can carry the device in a backpack or shoulder pack while carrying out activities of daily living.

Regulatory Status

The NovoTTF-100A™ System (assigned the generic name of tumor-treatment fields) was approved by the FDA in April 2011 through the premarket approval process. The FDA-approved indication for use is: “The NovoTTF-100A System is intended as a treatment for adult patients (22 years of age or older) with confirmed GBM, following confirmed recurrence in an upper region of the brain (supratentorial) after receiving chemotherapy. The device is intended to be used as a stand-alone treatment, and is intended as an alternative to standard medical therapy for recurrent GBM after surgical and radiation options have been exhausted.”

In September 2014, FDA approved a request for Novocure to change its product name from Novo-TTF-110A System to Optune™.

In October 2015, FDA expanded the indication for Novocure’s use of Optune in combination with temozolomide for newly diagnosed glioblastoma.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

Tumor treatment fields therapy to treat glioblastoma is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Tumor-Treatment Fields Therapy is covered

Not applicable.

When Tumor-Treatment Fields Therapy is not covered

Tumor treatment fields therapy to treat glioblastoma multiforme 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.
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Policy Guidelines

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.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: A4555, E0766*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


Specialty Matched Consultant – 9/2013

Senior Medical Director – 9/2013


BCBSA Medical Policy Reference Manual [Electronic Version], 1.01.29, 8/14/14
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BCBSA Medical Policy Reference Manual [Electronic Version], 1.01.29, 8/13/15


Policy Implementation/Update Information

10/1/13 New policy. Tumor treatment fields therapy to treat glioblastoma is considered investigational. Senior Medical Director review 8/30/2013. Specialty Matched Consultant review 9/18/2013. (btw)

12/10/13 Specialty Matched Consultant Advisory Panel review 11/20/2013. No change to policy statement. (btw)

12/31/13 Added new HCPCS codes, A4555 and E0766, to the Billing/Coding section. Removed the following statement from the Billing/Coding section; “Providers will most likely use E1399 and A9900 for claim submission.” (btw)

12/9/14 Specialty Matched Consultant Advisory Panel review 11/24/2014. No change to policy intent. Reference added. (lpr)

12/30/15 Updated Policy Guidelines. Specialty Matched Consultant Advisory Panel review 11/18/2015. Reference added. No change to policy statement. (lpr)


8/11/17 Updated Policy Guidelines section. Clarified policy statement: 1) 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; 2) as an adjunct to standard maintenance therapy in patients with newly diagnosed glioblastoma multiforme following initial treatment with surgery, radiotherapy and/or chemotherapy. No change to policy intent and the service remains investigational. Reference added. (lpr)

8/25/17 Under “When Not Covered” section: clarified investigational indications. No change to policy intent. (lpr)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.