This Protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following Protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals: • With advanced or recurrent glioblastoma multiforme</td>
<td>Interventions of interest are: • Tumor-treatment fields therapy as an alternative to standard chemotherapy</td>
<td>Comparators of interest are: • Standard chemotherapy</td>
<td>Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals: • With glioblastoma multiforme on maintenance therapy after initial treatment with surgery and/or radiotherapy</td>
<td>Interventions of interest are: • Tumor treatment fields therapy as an adjunct to standard maintenance therapy</td>
<td>Comparators of interest are: • Standard maintenance therapy alone</td>
<td>Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity</td>
</tr>
</tbody>
</table>

Description
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 the course of treatment. Tumor-treatment fields (TTF) therapy is a new noninvasive technology that is intended to treat glioblastoma using alternating electric fields.

Summary of Evidence
For individuals who have advanced or recurrent GBM who receive TTF therapy as an alternative to standard chemotherapy the evidence includes one randomized controlled trial (RCT) and nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. The single published RCT reported no differences in outcomes between patients treated with TTF and standard chemotherapy. This trial had numerous methodologic limitations. Comparisons made only included an active control of questionable efficacy, which may not reflect current standard of care. There was high dropout (more than 20% of patients in each group were lost to follow-up) and, for the quality of life outcomes, only approximately 25% of enrolled patients had complete data. The two 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 GBM on maintenance therapy after initial treatment with surgery and/or radiotherapy who receive TTF therapy as an adjunct to standard maintenance therapy, the evidence includes one 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**

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 advanced or recurrent glioblastoma multiforme
- As an adjunct to standard maintenance therapy in patients with glioblastoma multiforme following initial treatment with surgery and/or radiotherapy.

**Policy Guidelines**

The patient reappears the transducer arrays at home after the initial instruction.

**Medicare Advantage**

For Medicare Advantage tumor-treatment fields therapy is considered *not medically necessary*.

**Background**

*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 “deadliest brain tumor with only a third of patients surviving for one year and less than 5% living beyond five years.”\(^2\)

*Therapeutic Options*

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 (bis-chloroethylnitrosourea [BCNU])–impregnated wafer.\(^2\) Depending on the patient’s physical condition, adjuvant radiotherapy, 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 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 (e.g., irinotecan, BCNU/chloroethylnitrosourea [CCNU], temozolomide), temozolomide, nitrosourea, PCV (procarbazine, CCNU, vincristine), cyclophosphamide, and platinum-based agents.\textsuperscript{2} External beam radiotherapy (EBRT) also may be used to treat recurrent GBM. Response rates in recurrent disease are less than 10%, and progression-free survival rates at six months are less than 20%.\textsuperscript{2, 3}

**Tumor Treatment Fields Therapy**

TTF therapy is a new, noninvasive technology that is 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 to both selectively inhibit tumor growth and reduce tumor angiogenesis. TTF are proposed to inhibit rapidly dividing tumor cells by two mechanisms, arrest of cell proliferation and destruction of cells while undergoing division.\textsuperscript{4, 5}

The NovoTTF-100A™ System has received marketing approval from the U.S. Food and Drug Administration (FDA) to deliver TTF therapy. TTF therapy via the NovoTTF-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.\textsuperscript{3, 4} The device is used by the patient at home on a continuous basis (20-24 h/d) 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.\textsuperscript{3, 4}

**Regulatory Status**

In April 2011 the NovoTTF-100A™ System (Novocure, Haifa, Israel; assigned the generic name of TTF) was approved by FDA through the premarket approval process.\textsuperscript{6} The FDA-approved label reads as follows: “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.”\textsuperscript{6}

On September 28, 2014, FDA approved Novocure’s request to change its products name from NovoTTF-110A System to Optune™.\textsuperscript{7}

In October 2015, FDA expanded the indication for Novocure’s use of Optune in combination with temozolomide to include newly diagnosed GBM.\textsuperscript{8}

Product code: NZK.

**Related Protocols**

Intensity-Modulated Radiotherapy: Central Nervous System Tumors
Intracavitary Balloon Catheter Brain Brachytherapy for Malignant Gliomas or Metastasis to the Brain
Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*
It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

**References**

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


14. New Hampshire, New Jersey, New York - Entire State, Pennsylvania, Rhode Island, Vermont) Local Coverage Determination (LCD): Tumor Treatment Field Therapy (TTFT) (L34823), Revision Effective Date: For services performed on or after 10/01/2015.