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OVERVIEW

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.

MEDICAL CRITERIA

BlueCHiP for Medicare and Commercial Products:

Initial Coverage For Newly Diagnosed Glioblastoma Multiforme:

Tumor treatment field therapy (E0766) is covered for the treatment of newly diagnosed Glioblastoma Multiforme (GBM) only when all of the following criteria are met:

1. The member has histologically confirmed (World Health Organization (WHO) grade IV astrocytoma), newly diagnosed, supratentorial GBM; and,
2. The member has received initial treatment with maximal debulking surgery (when feasible), followed by chemotherapy and radiotherapy; and,
3. Tumor treatment field therapy is initiated within 7 weeks from the last dose of concomitant chemotherapy or radiotherapy, whichever is later; and,
4. The member has no evidence of progression by Response Assessment in Neuro-Oncology (RANO) criteria; and,
5. The beneficiary has a Karnofsky Performance Score (KPS) of at least 70; and,
6. The beneficiary will use TTF for an average of 18 hours per day.

APPROVAL PERIOD: 6 months. Services beyond the 6 months will need a new review and meet the above criteria.

***KARNOFSKY PERFORMANCE STATUS SCALE DEFINITIONS RATING (%) CRITERIA**

- 100 Normal no complaints; no evidence of disease.
- 90 Able to carry on normal activity; minor signs or symptoms of disease. Able to carry on normal activity and to work; no special care needed.
- 80 Normal activity with effort; some signs or symptoms of disease.
- 70 Cares for self; unable to carry on normal activity or to do active work.
- 60 Requires occasional assistance, but is able to care for most of his personal needs. Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.
- 50 Requires considerable assistance and frequent medical care.
- 40 Disabled; requires special care and assistance.
- 30 Severely disabled; hospital admission is indicated although death not imminent.
- 20 Very sick; hospital admission necessary; active supportive treatment necessary.
- 10 Moribund; fatal processes progressing rapidly. Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.
- 0 Dead

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare and recommended for Commercial Products

POLICY STATEMENT

BlueCHiP for Medicare and Commercial Products:

Tumor treating fields therapy is medically necessary when the above criteria is met.

Tumor treating fields therapy is considered not covered/not medically necessary in all other conditions, including but not limited to the following situations:

- As an adjunct to standard medical therapy (e.g. bevacizumab, chemotherapy) for patients with progressive or recurrent glioblastoma multiforme
- As an alternative to standard medical therapy for patients with progressive or recurrent glioblastoma multiforme
- For brain metastases
- For cancer in areas other than the brain.
- As an adjunct to standard medical therapy (pemetrexed and platinum-based chemotherapy) for patients with malignant pleural mesothelioma

COVERAGE

Benefits vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for services not medically necessary or not covered

BACKGROUND

Tumor treating fields (TTF) therapy is a noninvasive technology intended to treat glioblastoma and malignant pleural mesothelioma on an outpatient basis and at home using electrical fields. 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. Malignant pleural mesothelioma is an aggressive tumor with few treatment options that is associated with significant morbidity and mortality.

For individuals who have newly diagnosed GBM on maintenance therapy after initial treatment who receive TTF therapy as an adjunct to standard maintenance therapy, the evidence includes a randomized controlled trial (RCT). Relevant outcomes include overall survival, disease-specific survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. The EF-14 trial found a significant increase of 2.7 months in progression-free survival and an increase of 4.9 months in overall survival with the addition of TTF therapy to standard maintenance therapy (ie, temozolomide) in patients with newly diagnosed GBM. Although patients were not blinded to treatment assignment, progression-free survival was assessed by blinded evaluators, and the placebo effects on the objective measure of overall survival are expected to be minimal. This technology represents a clinically significant option in the treatment of patients with GBM, for whom options are limited. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have progressive or recurrent GBM who receive TTF therapy as an adjunct or alternative to standard medical therapy, the evidence includes an RCT and nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. The single RCT evaluating TTF therapy for recurrent GBM did not show superiority of TTF therapy for the primary outcome (overall survival) compared with physicians' choice chemotherapy. Because no serious adverse effects have been identified with TTF therapy, this raises the possibility that treatment with TTF might reduce the toxicity associated with treatment for recurrent GBM. A reduction in chemotherapy-associated toxicity without loss of efficacy would be considered a net health benefit. However, this RCT is not sufficient to permit conclusions on the efficacy of the device. Because the trial was not designed as a noninferiority trial, no inferences of noninferiority compared with chemotherapy can be made. Also, quality of life assessment was measured in an insufficient number of patients to reach firm conclusions on differences in quality of life between TTF therapy and medical treatment. The highest quality study of TTF combined with medical treatment for recurrent GBM is a post hoc analysis of the EF-14 trial. A high-quality,

prospective RCT is needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unresectable, locally advanced or metastatic, malignant pleural mesothelioma who receive TTF therapy as an adjunct to standard maintenance therapy, the evidence includes one single-arm observational study conducted in 80 patients. Relevant outcomes include overall survival, disease-specific survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. The study has not been published but is described in the FDA Summary associated with its Humanitarian Device Exemption designation. In patients who received TTF therapy in combination with pemetrexed and cisplatin or carboplatin, median overall survival was 18.2 months (95% CI 12.3 to 25.8 months). Because there was no comparison group, it is not possible to make conclusions about the effectiveness of the intervention compared to medical therapy alone. The evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Regulatory Status

In April 2011, the NovoTTF-100A™ System (Novocure; assigned the generic name of TTF) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. 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."

In September 2014, FDA approved Novocure's request for a product name change from NovoTTF-110A System to Optune®.

In October 2015, FDA expanded the indication for Optune® in combination with temozolomide to include newly diagnosed GBM. The device was granted priority review status in May 2015 because there was no legally marketed alternative device available for the treatment of newly diagnosed GBM, a life-threatening condition. In July 2016, a smaller, lighter version of the Optune® device, called the Optune® System (NovoTTF-200A System), received FDA approval.

The FDA-approved label for newly diagnosed GBM reads as follows: "This device is indicated as treatment for adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme (GBM). Optune™ with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy."

In May 2019, FDA expanded the indication for the NovoTTF™-100L System to include "treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy. The indication was modified from that granted for the Humanitarian Device Exemption designation to more clearly identify the patient population the device is intended to treat and in which the safety and probable benefit of the device is supported by the available clinical data."

CODING

BlueCHiP for Medicare and Commercial Products

The following code is medically necessary/covered when criteria is met.

E0766: Electrical stimulation device used for cancer treatment, includes all accessories, any type

The following code is covered when the service is approved

A4555: Electrode/transducer for use with electrical stimulation device used for cancer treatment, replacement only

RELATED POLICIES

None

PUBLISHED

Provider Update, February 2020

Provider Update, September 2018

Provider Update, September 2017

Provider Update, October 2016

Provider Update, April 2015

Provider Update, March 2014

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