Clinical Policy: Electric Tumor Treating Fields (Optune)

Reference Number: LA.CP.MP.145 Coding Implications
Date of Last Revision: 1/26 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Electric tumor treating fields (TTF), also known as alternating electric field therapy, are used for the treatment of glioblastoma, and are delivered by Optune Gio™ (NovoCure®), a portable medical device that generates low-intensity electric fields termed Tumor Treating Fields. TTF are believed to disrupt the rapid cell division exhibited by cancer cells with the alternating electrical fields applied to the brain through electrodes placed on the scalp. The device is worn throughout the day and attached to the head by electrodes which creates a low intensity, alternating electric field within the tumor that exerts physical forces on electrically charged cellular components, preventing the normal mitotic process and causing cancer cell death prior to division.

Policy/Criteria

I. It is the policy of Louisiana Healthcare Connections that tumor treating fields (TTF) therapy is **medically** necessary for adults ≥ 22 years when meeting one of the following:

A. Request is for an initial 90 days of TTF therapy and all of the following:
   1. One of the following indications:
      a. New diagnosis of glioblastoma, histologically confirmed, and all of the following:
         i. Glioblastoma is in the supratentorial region;
         ii. Member/enrollee has good performance status, as defined by a Karnofsky Performance Status rating of ≥ 60;
         iii. Alternating electric field therapy will be delivered in conjunction with temozolomide after standard surgical and/or radiation therapies have been completed;
      b. Recurrent glioblastoma, histologically- or radiologically- confirmed and both of the following:
         i. Glioblastoma is in the supratentorial region;
         ii. Member/enrollee has good performance status, as defined by a Karnofsky Performance status rating of ≥ 60;
         iii. Alternating electric field therapy will be used as a monotherapy, after standard treatment with chemotherapy, surgery, and/or radiation;
   2. None of the following contraindications:
      a. Implanted medical device such as deep brain stimulator, spinal cord stimulators, vagus nerve stimulators, pacemakers, defibrillators, or programmable shunts;
      b. Skull defect such as a missing bone with no replacement, or bullet fragment;
      c. Pregnancy;
      d. Known sensitivity to conductive hydrogels (e.g., gels used on electrocardiogram [ECG] stickers or transcutaneous electrical nerve stimulation [TENS] electrodes);
   3. The member/enrollee agrees to wear the TTF device for 18 hours per day;

B. Request is for an additional 90 days of therapy and both of the following:
   1. There has been no disease progression in the last 90 days of TTF therapy;

2. The member/enrollee agrees to wear the TTF device for 18 hours per day and was compliant with doing so in the prior authorization period.

II. It is the policy of Louisiana Healthcare Connections that there is insufficient evidence to support the use of TTF therapy for all other indications.

III. It is the policy of Louisiana Healthcare Connections that there is insufficient evidence to establish the efficacy of computer mapping software (NovoTal™) for planning TTF therapy.

Background

Optune Product Description

Optune, formerly NovoTTF-100A, produces alternating electrical fields within the human body that disrupt the rapid cell division exhibited by cancer cells, with the alternating electrical fields applied to the brain through transducer arrays placed on the scalp. Electric tumor treating fields (TTF) alter the tumor cell polarity at an intermediate frequency (on the order of 100 to 300 kHz). The frequency used for a particular treatment is specific to the cell type being treated (e.g., 200kHz for glioblastoma (GBM)). In contrast, the TTF have not been shown to have an effect on cells that are not undergoing division. Since most normal adult brain cells proliferate very slowly, if at all, they are hypothesized to be little affected by the TTF. Testing demonstrates no differences between treated and control animals in histology of the major internal organs (including the brain), blood examination, cardiac rhythm, body temperature, or in animal behavior. In addition, because the fields alternate so rapidly, they have no effect on normal quiescent cells nor do they stimulate nerves and muscles. It is noted that, because TTF are only applied to the brain, they have no effect on rapidly proliferating cells in the rest of the body. The intensities of the electric fields within the tissues are very small and do not result in any meaningful increase in tissue temperature. Thus, TTF application has the advantage of being highly selective and is not expected to be associated with significant toxicity.[1]

Optune Gio™, the second-generation NovoTTF-200A system, is smaller and lighter and allows for increased convenience and manageability. The transducer arrays did not change but post-marketing survey data in patients with GBM indicate that improved handling and portability helped patients comply with daily treatment duration goals for therapeutic efficiency. [19]

Position Statement

Guidelines from the National Comprehensive Cancer Network (NCCN) on central nervous system cancers, recommend alternating electrical fields therapy as a treatment option for newly diagnosed glioblastoma.[11] For patients with good performance status and either methylated or unmethylated/indeterminate O6-methylguanine-DNA methyltransferase (MGMT) promoter status, in conjunction with standard brain radiation therapy plus concurrent temozolomide and adjuvant temozolomide (category 1 recommendation- based on high- level evidence).[2] For recurrent glioblastoma, NCCN gives alternating electrical field therapy a 2B rating (consensus based upon lower-level evidence).[2]

Evidence for Optune

Initial United Stated Food and Drug Administration (FDA) approval for recurrent glioblastoma was based on Stupp et al.'s 2012 phase III clinical trial that randomized 237 patients to chemotherapy-free treatment of NovoTTF (20 to 24 hours per day) versus active chemotherapy in the treatment of patients with recurrent glioblastoma.[5] Primary end-point was improvement of overall survival. Patients were randomized to TTF alone or active chemotherapy control. Responses were more common in the TTF arm (14% versus 9.6%, p=0.19) and TTF-related adverse events were mild. Quality of life analyses favored TTF therapy in most domains. The investigators concluded that no improvement in overall survival was demonstrated. However, efficacy and activity with this chemotherapy-free treatment device appears comparable to chemotherapy regimens that are commonly used for recurrent glioblastoma. Toxicity and quality of life measures favored TTF.[11]

The FDA based its approval of the newly diagnosed glioblastoma indication of the Optune device on results from a 2015 clinical trial by Stupp et al.[4,5] The EF-14 trial included 695 patients newly diagnosed with glioblastoma (GBM) and compared those who used Optune with temozolomide to those receiving temozolomide alone. Patients who used the device along with temozolomide lived, on average, about seven months with no disease progression compared to four months for those who had the drug alone. The Optune plus temozolomide group survived for an average of 19.4 months after starting treatment compared to 16.6 months for those who were treated with only temozolomide.[5] One critique of this study is that the study was terminated at the pre-planned intermediate analysis due to success of the TTF treatment. With the newly diagnosed glioblastoma indication, Optune can be used for GBM before the disease progresses. For newly diagnosed GBM, Optune is not intended to be used as a substitute for standard treatments, but rather as an adjunct therapy, and should not be used without a physician's supervision.

Hayes conducted a review of the available literature on TTF, noting that overall the body of evidence was of fair to very poor quality, although it was consistently positive.[6] Hayes found the evidence to be stronger for the use of TTF for recurrent disease as opposed to newly diagnosed disease, as there were more supportive studies for recurrent disease at the time of publication (two vs. six). Out of the ten studies they reviewed, pertaining to the use of TTF in patients with GBM and select other cancers, two were of fair quality, and the other eight ranged from poor quality to very poor quality. The two fair quality trials were those conducted by Stupp et al. in 2012 and 2015, although these were noted to have limitations such as lack of a sham intervention and significant loss of follow up (22% and 20%, respectively).[6]

A post-hoc analysis of Stupp et al.'s E-14 trial of TTF plus temozolomide versus temozolomide alone in newly diagnosed glioblastoma compared the efficacy of TTF plus physician's choice of chemotherapy versus chemotherapy alone after first recurrence.[7] Median overall survival in the TTF plus chemotherapy was 11.8 months versus 9.2 months for the chemotherapy only group (p=.049).[7] TTF demonstrated low toxicity, consistent with previous studies. Limitations of this analysis are its post-hoc nature, as well as the crossover of 13 patients from the temozolomide only group to the TTF plus chemo group after approval and commercial availability of TTF for recurrent GBM.[7]

Vymazal et al. analyzed the response patterns in individuals who exhibited an objective response to TTF in two previous studies in order to evaluate the baseline characteristics of those individuals who responded and to evaluate the relationship between compliance with use and efficacy outcomes.[8] The analysis was completed on one pilot study (n=10) and a phase III trial (n=237) in which TTF was compared to standard chemotherapy. Between both studies, TTF was administered as monotherapy in 130 individuals. Across both trials, there was a 15% response rate (16/110 with a 4% complete response rate).[8] There were no significant differences in baseline characteristics between the responder and non-responder groups. In those in which a response was noted, there was frequently a delayed response, and the tumor would initially continue to grow before responding to treatment. Analysis supported that an increase in compliance was associated with better treatment response and longer overall survival. The extent of treatment response in those who exhibited a response was dependent on compliance ($p<0.001$).[8]

NovoTal
The NovoTal system (Novocure) is a computer software-planning tool that helps direct placement of transducer arrays for TTF therapy.[12] Few studies have evaluated outcomes of TTF planned by physicians with and without the use of NovoTal, and these are limited to a case series, physician use study, and two review articles. Additionally, many of the authors reported ties to Novocure.

Coding Implications
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2024, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only and may not support medical necessity. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

NOTE: Coverage is subject to each requested code's inclusion on the corresponding LDH fee schedule. Non-covered codes are denoted (*) and are reviewed for Medical Necessity for members under 21 years of age on a per case basis.

HCPCS Codes	Description
A4555	Electrode/transducer for use with electrical stimulation device used for cancer treatment, replacement only
E0766*	Electrical stimulation device used for cancer treatment, includes all accessories, any type

Reviews, Revisions, and Approvals	Revision Date	Approval Date	Effective Date
Converted corporate to local policy.	08/15/20		

Reviews, Revisions, and Approvals	Revision Date	Approval Date	Effective Date
Removed the phrase "not medically necessary" from criteria II. and III. References reviewed and updated. Annual review. Replaced I/E language in II & III "with insufficient evidence to support…"Changed "review date" in the header to "date of last revision" and "date" in the revision log header to "revision date." Added "and may not support medical necessity" to coding implications. References reviewed, updated and reformatted. Reviewed by specialist.	2/22		
Annual review. Added Criteria I.A.3. and Criteria I.B.2. to include that the member/enrollee agrees to wear the device 18 hours per day, and for continuation of therapy, has also been compliant with the wearing the device in the prior authorization period. Background updated with no impact on criteria. Removed ICD-10 codes. References reviewed and updated.	1/23	4/3/23	
Annual review. Updated wording in description with no impact to criteria. In I.A.1.a.iii. added "and/or"; in I.A.b.ii. changed wording to "chemotherapy, surgery, and/or radiation". References reviewed and updated. Reviewed by external specialist. Added note for non-covered codes.	1/24	3/25/24	
Annual review. Changed I.A.1.a.ii. From ≥ 60 to Karnofsky Performance Status of ≥ 70. Added I.A.1.b.ii. "Member has good performance status, as defined by a Karnofsky Performance status rating of ≥ 70. Updated description and background with no clinical significance. References reviewed and updated.	12/24	1/27/25	2/27/25
Annual review. Changed I.A.1.a.ii and b.ii. from KPS rating of ≥ 70 to ≥ 60. References reviewed and updated. Reviewed by external specialist.	1/26	3/30/26	4/30/26

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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