

VHA Office of Integrated Veteran Care
Community Care Medical Policy
Tumor Treating Fields (TTFs) Therapy

Policy Number: 00002

Effective Date: January 01, 2023

I. Important Information – Please read before using this policy

This policy is intended to be used as a reference for non-VA providers.

These guidelines do not guarantee benefits or constitute medical advice. This device is considered durable medical equipment (DME). Successful placement requires coordination between Community Care Provider, local facility Community Care office, and the Prosthetic and Sensory Aids Service (PSAS) department.

II. Community Care Medical Policy

a. Tumor Treating Fields Therapy

i. Indications for Tumor Treating Fields Therapy

FDA-approved Tumor Treating Fields (TTFs) therapy is considered medically necessary for the treatment of newly diagnosed Glioblastoma (GBM) and/or Grade 4 Astrocytoma when all of the following criteria are met:

- Beneficiary is 22 years or older; and
- Histologically confirmed GBM/Grade 4 Astrocytoma, newly diagnosed, supratentorial; and
- Initial treatment completed with maximal safe resection or biopsy, followed by concurrent chemotherapy and radiotherapy; and
- Administered with adjuvant Temozolomide, as tolerated; and
- TTFs therapy is initiated within 7 weeks from the last dose of concomitant chemotherapy or radiotherapy, whichever is the latter; and
- No evidence of progression by Response Assessment in Neuro-Oncology (RANO) criteria; and
- Karnofsky Performance Score (KPS) of at least 70 and/or Eastern Cooperative Oncology Group (ECOG) of 0 or 1; and

- Upon completion of required device training, the ability to apply/remove device, operate device (or caregiver) and use TTFs therapy for at least 18 hours per day.

The beneficiary will be monitored for 3 months for side effects and treatment tolerance. At the 60th day of treatment, but no later than the 91st day of TTFs treatment, providers will be required to evaluate effectiveness of treatment and determine the need for continued use.

ii. Limitations

The following are not considered reasonable and necessary and therefore will be denied:

- Use for indications other than newly diagnosed GBM/Grade 4 Astrocytoma
- Non-FDA-approved electric tumor, treatment field therapy

iii. Exclusion criteria

The following will exclude the Beneficiary from TTFs therapy:

- Cardiac pacemaker or implantable defibrillator
- Deep brain, spinal cord, or vagus nerve stimulator
- Major skull defect (e.g., missing bone)
- Metal within the brain (e.g., aneurysm clip, bullet fragment)
- Programmable ventriculoperitoneal shunt
- Pregnant, or trying to get pregnant

iv. Investigational or Experimental Treatment

Use of TTFs therapy is considered experimental, investigational and/or unproven for all indications other than listed above in Section II.a.i Indications for Tumor Treating Fields Therapy.

Investigational or experimental treatments are not generally approved treatments or services according to VA standards. However, treatments may be evaluated on a case-by-case basis to determine medical necessity and coverage.

Requests for investigational or experimental treatments may be submitted through the Request for Services (RFS) process using VA Form 10-10172, Community Care Provider-Request for Service Form, signed by the ordering provider, and must include accompany supporting medical documentation.

v. Research/Clinical Trials

Gliomas are a collection of tumors arising from the glia or their precursors within the central nervous system, and glioblastoma is the most aggressive and most common form of the 4 distinct grades of gliomas. The following outlines clinical research completed to increase long-term survival rates for individuals diagnosed with GBM/Grade 4 Astrocytoma.

- Stupp et al. (2017) evaluated whether TTFs improves progression-free and overall survival of newly diagnosed GBM with the addition of TTFs therapy plus Temozolomide maintenance treatment compared with Temozolomide alone, often referred to as the EF-14 study. The trial included 695 participants who had tumor resection and completed chemoradiation therapy. Of the 695 randomized patients, 637 (92%) completed the trial. The median progression-free survival from randomization was 6.7 months in the TTFs plus Temozolomide group and 4.0 months in the Temozolomide alone group. Median overall survival was 20.9 months in the TTFs plus Temozolomide group compared to 16.0 months in the Temozolomide alone group. 48% of TTFs plus Temozolomide group experienced systemic adverse events compared to 44% in the Temozolomide alone group. 52% of TTFs plus Temozolomide group experienced mild to moderate skin toxicity secondary to the transducer arrays, while no skin toxicity was reported in Temozolomide along group.

vi. Description of Treatment

FDA-approved Optune is a TTFs therapy delivered by insulated surface transducer arrays applied directly to the scalp, providing continuous low-intensity, alternating electric fields within the tumor. This action disrupts rapidly dividing cells, causing cancer cell death and halting tumor growth. The treatment is individualized by transducer array configuration for scalp placement in relation to the tumor site using magnetic resonance imaging (MRI) guidance.

A trained individual places four adhesive transducer array patches on the surface of a shaved scalp to deliver the tumor treating fields. The transducer arrays are then connected to the portable Optune device and battery pack. The transducer arrays

require a shaved scalp and patch replacement at least twice a week. The device should be in place, at a minimum, 18 hours a day. The transducer arrays and the device should never get wet. Bathing requires the transducer arrays be covered with a shower cap and disconnection of device.

vii. Required Clinical Information

Supporting documentation from medical records including but not limited to visit notes, prior chemotherapy and radiation therapy, Karnofsky Performance Status and/or ECOG results, diagnostic imaging, diagnostic studies, and the written order/prescription from the treating provider, including provider name, and National Provider Identifier (NPI) shall be provided upon request. For continued TTFs treatment beyond the initial 3 months, providers will be required to document objective outcome measures and evidence of adherence to therapy in the medical record. This documentation shall be provided upon request.

viii. Request for Durable Medical Equipment

- Community Providers will utilize the Request for Service Form 10-10172 to submit DME and/or Prosthetic requests to the local facility Community Care office.
- All DME sections of the Request for Service Form 10-10172 must be filled out to ensure proper facilitation of the DME requests. If the proper information is not submitted, the local facility Community Care office will be unable to proceed with the request which could cause a delay in patient care.

ix. Credentialing and Accreditation Standards

Treatment with an FDA-approved TTFs Therapy device requires the prescribing healthcare provider complete the required certification training provided by the manufacturer.

x. Health Care Procedural Coding Information

- 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.

xi. FDA Approval

Device General Name: Tumor Treatment Fields

Device Trade Name: Optune™ (formerly NovoTTF-100A™ System)

Applicant: Novocure, Inc.

Address: 195 Commerce Way, Portsmouth, NH 03801

Date of Panel Recommendation: Not Applicable (for newly diagnosed GBM)

PMA Number: P100034/S013

Date of FDA Notice of Approval: October 5, 2015

Approval: [Approval Order](#)

The original PMA (P100034) was approved on April 8, 2011

Device: NOVOCURE LTD'S NOVOTTF-100A TREATMENT KIT

Generic Name: Stimulator, Low Electric Field, Tumor Treatment

Applicant: Novocure GmbH

Address: Park 6, Ch-6039 Root D4

PMA Number: P100034

Date Received: 08/16/2010

Decision Date: 04/08/2011

Notice Date: 05/06/2011

Approval: [Approval Order](#)

Supplements: S017 S002 S010 S014 S009 S015 S001 S018

S008 S004 S005 S016 S006 S013 S007 S019 S020 S021 S022

S003 S023 S011 S012 S025 S026 S027 S028

xii. Medicare Coverage

Available Medicare coverage determinations are listed below as a resource. This does not indicate VA exclusively follows CMS coverage determinations.

- National Medicare Coverage Position
 - NA
- Local Medicare Coverage Determination
 - CGS Administrations, LLC
 - Noridian Healthcare Solutions, LLC

III. Background

If untreated, GBM/Grade 4 Astrocytoma can quickly grow and spread throughout the central nervous system. Standard treatment modalities include maximal-safe surgical resection, followed by radiotherapy with concurrent temozolomide and 6-12 months of adjuvant chemotherapy. TTFs has been considered the fourth treatment modality after surgery, radiotherapy, and temozolomide treatment. The

FDA-approved TTFs therapy provided an additional modality to the current treatment options, increasing the progression-free survival time and overall survival without added systemic toxicity if used in the adjuvant phase.

CNS tumor grading has been based exclusively on histological features, but certain molecular markers can now provide powerful prognostic information. In the 2016 WHO classification, IDH-mutant diffuse astrocytic tumors were assigned to 3 different tumor types (Diffuse astrocytoma, Anaplastic astrocytoma, and Glioblastoma) depending on histological parameters. This has been most recently updated in the fifth edition of the WHO Classification of Tumors of the Central Nervous System (CNS), published in 2021. Importantly, Astrocytoma, IDH-mutant now covers grades 2-4 and eliminates the term “Glioblastoma, IDH-mutant.”

IV. Definitions

Terms	Definitions
Glioblastoma (GBM)	A highly malignant, rapidly growing type of brain tumor that arises from glial cells in the brain. There may be instances when the histological appearance does not meet criteria for GBM, but molecular data are consistent with GBM. These may be called “molecular GBM” and are considered GBM since they require the same treatment and run a similar clinical course.
Grade 4 Astrocytoma	In 2021 the WHO updated the criteria for GBM classification. What was previously called GBM may now fall under a new category of IDH mutant, grade 4 Astrocytoma. These can be histologically similar to GBM and managed the same, but their prognosis is slightly better given the presence of an IDH mutation.
Karnofsky Performance Score (KPS)	An assessment tool for functional impairment. It can be used to compare effectiveness of different therapies and to assess the prognosis in individual patients. In most serious illnesses, the lower the Karnofsky score, the worse the likelihood of survival.

Terms	Definitions
ECOG Performance Status Scale	The Eastern Cooperative Oncology Group (ECOG) performance status scale measures a patient’s level of functioning to care for themselves, perform daily activity, and individual physical ability.
Response Assessment in Neuro-Oncology (RANO) criteria	Radiographic criteria to assess response to treatment. Divides responses into four types of response based on MRI and clinical features; complete response, partial response, stable disease, and progression.
Supratentorial	The area located above the tentorium cerebelli, comprised of the cerebrum, ventricles, choroid plexus, pineal gland, hypothalamus, pituitary gland, and optic nerve.
Temozolomide	Alkylating antineoplastic agent used to treat specific types of brain cancer (e.g., glioblastoma, anaplastic astrocytoma).
Central nervous system	The part of the nervous system consisting of neurons, axons and supporting tissue that constitute the brain and spinal cord.

V. References

Stupp R, Taillibert S, Kanner A, et al. Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients with Glioblastoma: A Randomized Clinical Trial. JAMA. 2017;318(23):2306–2316. doi:10.1001/jama.2017.18718

U.S. Food and Drug Administration (FDA) Premarket Approval (PMA) for Novocure LTD’s NOVOTTF-100A Treatment Kit. PMA number P100034. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100034>

U.S. Food and Drug Administration (FDA) Premarket Approval (PMA) for Optune (Formerly the NOVOTTF-100A System). PMA number P100034/S013. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100034_S013

Centers for Medicare and Medicaid Services (CMS). Tumor Treatment Field Therapy (TTFT) Local Coverage Determination (LCD), ID # L34823.

<https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34823&ver=27&keyword=tumor%20treating%20fields&keywordType=starts&areald=all&docType=NCA,CAL,NCD,MEDCAC,TA,MC,D,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1>

Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A, Ellison DW. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol.* 2021 Aug 2;23(8):1231-1251. doi: 10.1093/neuonc/noab106. PMID: 34185076; PMCID: PMC8328013.

VI. Policy History/Revision Information

- a. Explanation of changes to Policy
- b. Link to previous versions
- c. Table of Applicable Dates

Revision Type	Date of Revision	Update(s) Made to Community Care Medical Policies
Original Effective Date	01/01/23	Development
Content Updates	03/21/23	Updated sections <ul style="list-style-type: none"> • II.a.iv - Investigational or Experimental Treatment • II.a.xii - Medicare Coverage
Last Review Date	NA	NA

VII. Instructions for Use

This policy is to be used as a reference and not intended to replace clinical judgement when determining care pathways.