

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Glioblastomas (or glioblastoma multiforme, astrocytoma, GBM) are rare, complex, deadly, and treatment-resistant cancers that comprise 50.1% of all primary malignant brain tumors (National Brain Tumor Society 2024). Approximately 14,490 people are expected to be diagnosed with glioblastoma in the United States in 2023, with a mean age at diagnosis of 65 and rare occurrence in children (National Brain Tumor Society 2024). The risk of glioblastoma increases significantly with age; however, the incidence has remained stable over the last 20 years among older adults. According to DynaMed (2024), "the age-adjusted annual incidence is about 3 per 100,000 persons, with higher rates in persons \geq 55 years old." Approximately 10,000 people in the United States die annually due to glioblastomas (National Brain Tumor Society 2024). The 5-year survival rate for glioblastoma is approximately 6.9%, with an average survival time of only 8 months, which has remained stable for decades (National Brain Tumor Society 2024). In the United States, rates are slightly higher among men than women. Caucasians have the highest rate of glioblastoma diagnoses compared to African Americans, Asians, and American Indians (NORD 2023).

Glioblastomas are graded on a scale from I to IV to determine the rate of tumor growth. Grade I is indicative of slow growth, whereas grade IV is indicative of rapid growth. It is common for glioblastomas to begin as grade IV tumors without first progressing from grade I to grade IV. Typically, glioblastomas do not spread from the brain; however, they can be located anywhere in the brain (NORD 2023). Symptoms include headaches, seizures, confusion, memory loss, muscle weakness, visual changes, language deficits, and cognitive changes. Treatment options include a combination of surgery, chemotherapy, radiation therapy, and alternating electric field therapy (NORD 2023). While glioblastoma was identified in the medical literature in the 1920s, only four drugs and one device have been approved by the Food and Drug Administration (FDA); none of the available treatments have successfully extended a patient's life beyond a few additional months. These treatments can impact parts of the brain that control cognition, mood, behavior, and all other functions of every organ and body part. As a result, patients lose the ability to work and carry out daily activities that contribute to their independence and sense of self (National Brain Tumor Society 2024).

The standard of care for newly diagnosed patients with glioblastoma is debulking surgery followed by combination chemotherapy using temozolomide and radiation therapy. Essentially all newly diagnosed patients relapse despite the best available treatment (median time to recurrence of approximately 7 months). At the time of recurrence, treatment options for patients are limited. Approximately 20% of patients may undergo repeat surgery. Carmustine polymer wafers may be placed intraoperatively in the surgical cavity during repeat surgery to improve survival. Rarely, patients may undergo reirradiation. For the majority of recurrent patients, chemotherapy is indicated. In the United States, combination treatment with chemotherapy and the angiogenesis inhibitor bevacizumab has been approved for recurrent glioblastoma and certain other cancers. However, 40-60% of recurrent patients are either unresponsive to bevacizumab or experience serious adverse events following treatment (¹⁻³Bachtelor 2023).

Electric tumor treatment fields, also known as alternating electric field therapy and tumor treatment field therapy (TTFT), is a non-invasive anticancer modality that is comprised of low-intensity (1–3 V/cm) and intermediate-frequency (100–300 kHz), alternating electric fields delivered via cutaneous transducer arrays that are configured to provide optimal tumor-site coverage (Rominiyi et al., 2021). The procedure is performed using Novocure (Optune™ or NovoTFF-100A System), which emits alternating electric fields that disrupt the rapid cell division exhibited by cancer cells. Novocure has been approved for use in patients with recurrent glioblastoma or as a concomitant treatment with

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temozolomide in patients with newly diagnosed glioblastoma. The Optune™ system is intended to treat patients with glioblastoma by using transducer arrays placed on the patient's scalp according to the tumor's location. Patients use the device on an outpatient basis for at least 18 hours per day for 4 weeks to several months. Intended benefits include stabilizing the disease, having fewer treatment-related adverse events, and improving quality of life. A potential disadvantage is skin irritation (Optune 2023, 2019).

Regulatory Status

The NovoTTF-100A device received premarket approval from the Food and Drug Administration (FDA) on April 8, 2011, as a Class 3 device under Product Code NZK for the treatment of patients with recurrent glioblastoma multiforme (FDA 2011). Approval was extended to patients with newly diagnosed glioblastoma in combination with temozolomide in 2015 (FDA 2015). The NovoTTF-100A device received an FDA-approved name change to the Optune on September 28, 2014 (FDA 2014). A subsequent FDA-approved name change to the Optune Gio was approved on August 14, 2023 (FDA 2023).

COVERAGE POLICY

Electric Tumor Treatment Field Therapy, when used according to FDA labeled indications, contraindications, warnings, and precautions, **may be considered medically necessary** when **ALL** of the following criteria are met:

1. Initial request is for 90 days of electric tumor treatment field therapy.
2. Member is age 22 years or older.
3. Member can adhere to therapy that includes treatment to be provided by a trained individual or caregiver that can apply the device daily and Member is willing to wear the device at least 18 hours per day.
4. Member has a diagnosis of glioblastoma with a World Health Organization grade IV astrocytoma that is **newly diagnosed** as indicated by **ALL** of the following:
 - a. Administered in combination with temozolomide.
 - b. Initial treatment with maximal debulking surgery (when feasible), followed by chemotherapy and radiotherapy.
 - c. Supratentorial disease.
5. Karnofsky Performance Status (KPS) score of 60 or higher.
6. Member has **NONE** of the following contraindications:
 - a. Cardiac pacemaker or implantable defibrillator
 - b. Deep brain, spinal cord, or vagus nerve stimulator
 - c. Major skull defect (e.g., missing section of calvarium)
 - d. Metal within brain (e.g., aneurysm clip, bullet fragment)
 - e. Programmable ventriculoperitoneal shunt
 - f. Pregnancy
 - g. Known sensitivity to conductive hydrogels (e.g., gels used on electrocardiogram stickers or transcutaneous electrical nerve stimulation electrodes)

Recurrent Glioblastoma

Electric tumor treatment field therapy **may be considered medically necessary** for recurrent glioblastoma for an initial three-month period when the above criteria are met.

Continuation of electric tumor treatment field therapy for recurrent glioblastoma is dependent on **ALL** of the following:

- Member has had a magnetic resonance imaging scan ≤ 2 months prior to the request and there is no evidence of disease progression.
- Member with newly diagnosed glioblastoma continues to receive Temozolomide.
- Karnofsky Performance Score score of ≥ 60 or Eastern Cooperative Oncology Group Performance Status ≤ 2.

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- Documentation indicating that the Member has been using the device \geq 18 hours a day.

Continuation of Therapy

Continued treatment beyond the first THREE months (90 days) after initiating therapy **may be considered medically necessary** when the following criteria is met:

1. Member must have a face-to-face clinical re-evaluation by the treating Provider that indicates benefit from the treatment as documented by **ALL** of the following:
 - a. Magnetic resonance imaging scan performed two (2) to four (4) months prior to request that shows no evidence of disease progression.
 - b. Karnofsky Performance Score of \geq 60.
 - c. Documentation of compliance that the Member has been compliant and wears the device at least 18 hours per day.

Limitations and Exclusions

Electric tumor treatment field therapy **is considered experimental and investigational** due to a lack of evidence for any indication not listed above. This includes, but is not limited to:

- Treatment of tumors other than glioblastoma. *This policy only applies to the use of tumor treatment field therapy for glioblastoma. For other indications, please refer to the utilization management review hierarchy.*
- Use of electric tumor treatment field therapy with concurrent medical therapy (e.g., bevacizumab or chemotherapy) for treatment of recurrent glioblastoma.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The body of evidence is sufficient to determine that TTFT in patients with newly diagnosed glioblastoma demonstrates a health benefit. Clinical trials have shown that TTFT with temozolomide have a median overall survival that is longer than temozolomide alone. Medical literature for TTFT is insufficient to determine net health benefits in recurrent glioblastoma. Evidence is limited to small and individual studies with serious limitations, including lack of a control or comparator group, high loss to follow-up, and lack of statistical comparisons. Randomized controlled trials and cohort studies of sufficient size and design are needed to further investigate the safety and efficacy of TTFT in patients with recurrent glioblastoma.

Ballo et al. (2023) completed a meta-analysis and systematic review to determine “whether a constant survival benefit has been observed in the real-world setting, and whether device usage has played a role.” Researchers included studies that evaluated overall survival in patients with newly diagnosed glioblastoma treated with TTFT. A total of seven studies comparing TTFT in addition to chemoradiotherapy (standard of care) to chemoradiotherapy alone were included in the pooled analysis. The seven studies included a total of 1430 patients with 748 treated with TTFT and chemoradiotherapy and 682 treated with chemoradiotherapy alone. The median age of those treated with TTFT and chemoradiotherapy ranged from 48-61 years compared to 48-65 years for those treated with chemoradiotherapy alone. Maximum age ranges were 63-81 for those treated with TTFT and chemoradiotherapy compared to 75-83 years for those treated with chemoradiotherapy alone. Pooled results for overall survival were reported as percentages at two-years and four-years. In addition, the median overall survival was reported in number of months. The overall survival rates for those treated with TTFT and chemoradiotherapy were 46.8% at 2-years and 22.7% at 4-years compared to 32.3% at 2-years and 8.0% at 4-years for those treated with chemoradiotherapy alone. Median overall survival was 22.6 months for TTFT combined with chemoradiotherapy and 17.4 months for chemoradiotherapy alone. Researchers noted that improved survival rates were noted in the TTFT with chemoradiotherapy group when the average device usage was \geq 75% ($p < 0.001$).

Rominiyi et al. (2021) reviewed the mechanisms by which TTFT mediates anticancer effects. There is minimal research on the pediatric population with respect to the use of chemotherapy and radiotherapy. Research shows that TTFT shows a broad mechanism of action by interrupting a multitude of biological processes (DNA repair, cell permeability and immunological responses, to elicit therapeutic effects). Efficacy was also found in pediatric patients diagnosed with glioblastoma. One study demonstrated that TTFT were tolerable in five pediatric patients with high-grade glioma between the ages 10-20. Three studies demonstrated partial responses when TTFT was paired with chemotherapy and/or radiation. For adults with newly diagnosed glioblastoma, improvements lead to an expected survival of under two years.

Ghiaseddin et al. (2020) reported on the efficacy and tolerance of TTFT in patients with glioblastoma that were studied in two large phase 3 trials. Adherence was reported 75% of the time despite the need for patients to regularly shave their head. Increased survival corresponded with level of usage.

Shah et al. (2020) conducted a systematic review that evaluated prior studies on the efficacy of TTFT in patients with high-grade gliomas. A total of 852 studies conducted through February 2019 were initially reviewed for inclusion however, nine were included in the final review (two pilot clinical trials, two randomized clinical trials, and five retrospective studies). There were 1191 patients identified who received TTFT. Increased survival was noted among newly diagnosed glioblastoma patients however, this increase was not noted for recurrent glioblastoma patients.

Toms et al. (2019) analyzed compliance data from TTFT and temozolomide patients in a subgroup analysis of the phase 3 EF-14 trial by Stupp et al. (2017). The aim was to correlate TTFT compliance with progression free survival, overall survival, and to identify potential lower boundary for compliance with improved clinical outcomes. Compliance was assessed by usage data from the NovoTTF-100A device and calculated as percentage per month of TTFT delivery. TTFT/temozolomide patients were segregated into subgroups by percent monthly compliance. A Cox proportional hazard model controlled for sex, extent of resection, MGMT methylation status, age, region, and performance status was used to investigate the effect of compliance on progression free survival and overall survival. A threshold value of 50% compliance with TTFT/temozolomide improved progression free survival and overall survival versus temozolomide alone with improved outcome as compliance increased. With a compliance of >90%, median survival was 24.9 months (28.7 months from diagnosis); the five-year survival rate was 29.3%. In conclusion, a compliance threshold of 50% with TTFT/temozolomide correlated with significantly improved outcome survival and progression free survival versus temozolomide alone. Hence, the evidence supports that the use of TTFT in recurrent GBM is associated with improved overall survival when used consistently with a trend towards higher levels of survival associated with increasing compliance.

Tophoorn et al. (2018) completed a secondary analysis of the Stupp et al. (2017) trial with the goal of examining the association of TTFT with progression-free survival and health-related quality of life among patients with glioblastoma. Of the 695 patients in the study, 639 (92%) completed the baseline health-related quality of life questionnaire. Of these, 437 (68%) were men; mean age was 54.8 (11.5) years. The health-related quality of life did not differ significantly between treatment arms except for itchy skin. Deterioration-free survival was significantly longer with TTFT for global health (4.8 vs 3.3 months); physical (5.1 vs 3.7 months) and emotional functioning (5.3 vs 3.9 months); pain (5.6 vs 3.6 months); and leg weakness (5.6 vs 3.9 months). These likely related to improved progression-free survival. Time to deterioration (reflecting the influence of treatment) did not differ significantly except for itchy skin (TTFT worse; 8.2 vs 14.4 months) and pain (TTFT improved; 13.4 vs 12.1 months). Role, social, and physical functioning were not affected by TTFT. The addition of TTFT to standard treatment with temozolomide for patients with glioblastoma resulted in improved survival without a negative influence on health-related quality of life except for increased itchy skin, an expected consequence from the transducer arrays.

Active Studies

Two related studies are currently recruiting in the United States. The first study is titled *Temozolomide with Radiation Therapy and Tumor Treating Fields Therapy in Treating Participants for Glioblastoma* (NCT03477110). This involves the use of the NovoTTF-200A device and the study location is the Sidney Kimmel Cancer Center at Thomas Jefferson University in Philadelphia, Pennsylvania. A second study, *Niraparib/TTF in GBM* (NCT04221503), is also recruiting in Philadelphia at the Hospital of the University of Pennsylvania. This study involves the Optune device (ClinicalTrials.gov 2024).

National and Specialty Organizations

The **National Comprehensive Cancer Network (NCCN)** (2023) has published a clinical practice guideline related to cancers of the central nervous system. Each treatment pathway is based on the World Health Organization (WHO) grading system for each type of central nervous system tumor, the calculated Karnofsky Performance Score, and patient age (for select cancers). The NCCN recommends enrolling eligible patients into clinical trials as the first step for most treatment pathways. Treatment recommendations for brain tumors include surgical resection (if feasible), radiation therapy, and/or chemotherapy as treatment options. In addition, the NCCN makes the following recommendations regarding the use of electric TTFT:

- The NCCN denotes electric TTFT “is only an option for patients with supratentorial disease” for all treatment options that include electric TTFT.
- **WHO grade 4s IDH-mutant astrocytoma:** Electric TTFT with temozolomide can be considered as a concurrent or adjuvant therapy to standard radiotherapy for patients with a good performance score (Karnofsky Performance Score \geq 60) (category 2A recommendation).
- **Methylated, indeterminate, or unmethylated glioblastoma and age \leq 70 years:** Standard radiotherapy with concurrent temozolomide and adjuvant temozolomide with electric TTFT can be considered as a treatment option for patients with a good performance score (Karnofsky Performance Score \geq 60) (category 1 recommendation). The NCCN denotes that the “combination of modalities may lead to increased toxicity or radiographic changes.” The NCCN also notes this is the preferred treatment pathway for this patient population.
- **Methylated, indeterminate, or unmethylated glioblastoma and age $>$ 70 years:** Standard radiotherapy with concurrent temozolomide and adjuvant temozolomide with electric TTFT can be considered as a treatment option for patients with a good performance score (Karnofsky Performance Score \geq 60) who wish to be treated as aggressively as possible (category 1 recommendation). The NCCN denotes that the “combination of modalities may lead to increased toxicity or radiographic changes.” The NCCN places preference on enrollment in clinical trials for eligible patients in this patient population.
- **Recurrent or progressive glioblastoma:** Electric TTFT may be considered for glioblastoma (diffuse/multiple or local) (category 2B recommendation). Preference is given to participation in a clinical trial or resection prior to electric TTFT if a local recurrence is resectable.

The **American Society of Clinical Oncology (ASCO)** and the **Society for Neuro-Oncology (SNO)** published guidelines for therapies for diffuse astrocytic and oligodendroglial tumors in adults (Mohile et al. 2022). The guidelines recommend that TTFT “may be added to adjuvant [temozolomide] in people with newly diagnosed supratentorial glioblastoma, IDH-wildtype, [central nervous system] WHO grade 4 who have completed chemoradiation therapy.” The recommendation is based on a “moderate” quality of evidence with a “weak” strength of recommendation.

The **Congress of Neurological Surgeons (CNS)** published guidelines for the role of cytotoxic chemotherapy and other therapies in the management of *progressive* glioblastoma in adults (Germano et al. 2022). The guidelines state that TTFT may be considered when used in conjunction with chemotherapy. However, “there is insufficient evidence to recommend [TTFT] to increase overall survival in adult patients with [progressive glioblastoma].” The recommendation is graded as level III.

The **Congress of Neurological Surgeons (CNS)** also published guidelines for the role of “emerging developments” in the management of *newly diagnosed* glioblastoma (Farrell et al. 2020). The guidelines state “the use of [TTFT] is recommended for patients with newly diagnosed glioblastoma who have undergone debulking and completed concurrent chemoradiation without progression of disease at the time of [TTFT] initiation.” The recommendation is graded as level II.

SUPPLEMENTAL INFORMATION**Definitions (NCI date unknown):**

Karnofsky Performance Status (KPS): A standard way of measuring the ability of cancer patients to perform ordinary tasks; KPS scores range from 0 to 100 (a higher score means a person is better able to carry out daily activities). For example, a KPS of 60 means a person requires occasional assistance but is able to care for most of their personal needs. KPS may be used to determine a patient’s prognosis, to measure changes in a patient’s

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ability to function, or to decide if a patient could be included in a clinical trial.

Response Assessment in Neuro-Oncology (RANO): Progression criteria is defined as $\geq 25\%$ increase in enhancing disease or worsening neurologic status in the setting of stable or increasing steroid use.

upratentorial: The upper portion of the brain comprised of the cerebrum, ventricles, choroid plexus, hypothalamus, pineal gland, pituitary gland, and optic nerve. Examples of tumors that form in the supratentorium are glioblastomas, pineal region tumors, and ependymomas.

Temozolomide: Also called Temodar. An oral alkylating chemotherapy drug used in the treatment of some brain cancers and is considered a first-line treatment for glioblastoma.

CODING & BILLING INFORMATION

NOTE: CMS does not have a National Coverage Determination (NCD) for electric tumor treatment field therapy however, there is a Local Coverage Determination (LCD) (L34823) for Tumor Treatment Field Therapy (TTFT). Effective 10/1/2015; revision effective date 1/1/2020.

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	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

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

02/14/2024	Policy reviewed, no changes to criteria. Updated Overview, Summary of Medical Evidence, and References. IRO Peer Review on January 31, 2024, by a practicing, board-certified physician with a specialty in Medical Oncology.
02/08/2023	Policy reviewed, no changes to criteria, updated references.
02/09/2022	Policy reviewed; TTF now covered for recurrent glioblastoma; updated Summary of Medical Evidence and Reference sections.
02/08/2021	Policy reviewed, no changes to criteria.
04/23/2020	New policy. IRO Peer Review in January 2020 by a practicing, board-certified neurologist.

REFERENCES

- Ballo MT, Conlon P, Lavy-Shahaf G, et al. Association of tumor treating fields (TTFields) therapy with survival in newly diagnosed glioblastoma: A systematic review and meta-analysis. *J Neurooncol.* 2023 Aug;164(1):1-9. Doi: 10.1007/s11060-023-04348-w. Epub 2023 Jul 26. PMID: 37493865; PMCID: PMC10462574.
- ¹Batchelor T. Initial treatment and prognosis of IDH-wildtype glioblastoma in adults. Updated May 24, 2023. Accessed December 19, 2023. www.uptodate.com.
- ²Batchelor T, Shih HA. Management of glioblastoma in older adults. Updated August 15, 2023. Accessed January 23, 2024. www.uptodate.com.
- ³Batchelor T, Shih H, Carter B. Management of recurrent high-grade gliomas. Updated December 11, 2023. Accessed January 23, 2024. www.uptodate.com.
- Centers for Medicare and Medicaid Services (CMS). Medicare coverage database: Local coverage determination – Tumor treatment field therapy (L34823). Revision effective January 1, 2020. Accessed December 19, 2023. <https://www.cms.gov/medicare-coverage-database/search.aspx>.
- ClinicalTrials.gov. Temozolomide with radiation therapy and tumor treating fields therapy in treating participants for glioblastoma (NCT03477110), Niraparib/TTF in GBM (NCT04221503). National Library of Medicine. Accessed January 24, 2024. www.clinicaltrials.gov.
- DynaMed. Glioblastoma. EBSCO Information Services. Updated January 24, 2024. Accessed January 26, 2024. www.dynamed.com.
- Farrell C, Shi W, Bodman A, et al. Congress of Neurological Surgeons systematic review and evidence-based guidelines update on the role of emerging developments in the management of newly diagnosed glioblastoma. *J Neurooncol.* 2020 Nov;150(2):269-359. Doi: 10.1007/s11060-020-03607-4. Epub 2020 Nov 19. PMID: 33215345.
- Germano IM, Ziu M, Wen P, Ormond DR, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines update on the role of cytotoxic chemotherapy and other cytotoxic therapies in the management of progressive glioblastoma in adults. *J Neurooncol.* 2022 Jun;158(2):225-253. Doi: 10.1007/s11060-021-03900-w. Epub 2022 Feb 23. PMID: 35195819.

10. Ghiaseddin AP, Shin D, Melnick K, et al. Tumor treating fields in the management of patients with malignant gliomas. *Curr Treat Options Oncol.* 2020 Jul 30;21(9):76. Doi: 10.1007/s11864-020-00773-5. PMID: 32734509; PMCID: PMC7391234.
11. Mohile NA, Messersmith H, Gatson NT, et al. Therapy for diffuse astrocytic and oligodendroglial tumors in adults: ASCO-SNO Guideline. *J Clin Oncol.* 2022 Feb 1;40(4):403-426. Doi: 10.1200/JCO.21.02036. Epub 2021 Dec 13. PMID: 34898238.
12. National Brain Tumor Society. About glioblastoma. Updated 2024. Accessed January 24, 2024. <https://braintumor.org/events/glioblastoma-awareness-day/about-glioblastoma/>.
13. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology: Central nervous system cancers (version 1.2023) Published March 24, 2023. Accessed January 24, 2024. https://www.nccn.org/guidelines/category_1.
14. National Cancer Institute (NCI). Dictionary of cancer terms. Accessed January 2024. <https://www.cancer.gov/publications/dictionaries/cancer-terms/>.
15. National Organization for Rare Disorders (NORD). Rare disease database: Glioblastoma. Updated November 17, 2023. Accessed December 20, 2023. www.rarediseases.org.
16. Optune. Mechanism of action. Updated November 2023. Accessed January 24, 2024. <https://www.optunegiohcp.com/mechanism-of-action>.
17. Optune. Instructions for use. Published 2019. Accessed January 23, 2024. <https://www.optunegio.com/instructions-for-use>.
18. Rominiyi O, Vanderlinden A, Clenton SJ, et al. Tumour treating fields therapy for glioblastoma: Current advances and future directions. *Br J Cancer.* 2021 Feb;124(4):697-709. Doi: 10.1038/s41416-020-01136-5. Epub 2020 Nov 4. Erratum in: *Br J Cancer.* 2021 Aug;125(4):623. PMID: 33144698; PMCID: PMC7884384.
19. Shah PP, White T, Khalafallah AM, et al. A systematic review of tumor treating fields therapy for high-grade gliomas. *J Neurooncol.* 2020 Jul;148(3):433-443. Doi: 10.1007/s11060-020-03563-z. Epub 2020 Jun 23. PMID: 32578135.
20. 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 Dec 19;318(23):2306-2316. Doi: 10.1001/jama.2017.18718. Erratum in: *JAMA.* 2018 May 1;319(17):1824. PMID: 29260225; PMCID: PMC5820703.
21. Taphoorn MJB, Dirven L, Kanner AA, et al. Influence of treatment with tumor-treating fields on health-related quality of life of patients with newly diagnosed glioblastoma: A secondary analysis of a randomized clinical trial. *JAMA Oncol.* 2018 Apr 1;4(4):495-504. Doi: 10.1001/jamaoncol.2017.5082. PMID: 29392280; PMCID: PMC5885193.
22. Toms SA, Kim CY, Nicholas G, et al. Increased compliance with tumor treating fields therapy is prognostic for improved survival in the treatment of glioblastoma: A subgroup analysis of the EF-14 phase III trial. *J Neurooncol.* 2019 Jan;141(2):467-473. Doi: 10.1007/s11060-018-03057-z. Epub 2018 Dec 1. PMID: 30506499; PMCID: PMC6342854.
23. United States Food and Drug Administration (FDA). Premarket approval (PMA): Supplement for name change (P100034/S031). Published August 14, 2023. Accessed January 26, 2024. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.
24. United States Food and Drug Administration (FDA). Premarket approval application (PMA): Supplement for the Optune™ (formerly the NovoTTF-100A System) (P100034/S013). Published October 5, 2015. Accessed January 23, 2024. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.
25. United States Food and Drug Administration (FDA). Premarket approval (PMA): Supplement for name change (P100034/S010). Published September 28, 2014. Accessed January 26, 2024. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.
26. United States Food and Drug Administration (FDA). Premarket approval application (PMA): NovoTTF- IOOA System (P100034). Published April 8, 2011. Accessed January 23, 2024. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.