BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 09/19/22**
SECTION: DURABLE MEDICAL EQUIPMENT	**LAST REVIEW DATE: 09/03/24**
	CURRENT EFFECTIVE DATE: 09/03/24
	LAST CRITERIA REVISION DATE: 09/21/23
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

TUMOR TREATING FIELDS THERAPY

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

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 treatment. Malignant pleural mesothelioma is an aggressive tumor with few treatment options that is associated with significant morbidity and mortality.

Prognostic factors for therapy success are age, histology, performance status or physical condition of the individual, and extent of resection. National Comprehensive Cancer Network recommendations include individual age and Karnofsky Performance Status score as important determinants of postsurgical treatment choice. For individuals with good performance status, the most aggressive treatment (standard radiotherapy [RT] plus temozolomide) is recommended. For individuals with poor performance status, only single treatment cycles or even palliative or supportive care are recommended. Hypofractionated RT is indicated for individuals with poor performance status because it is better tolerated, and more individuals are able to complete RT.

Treatment of GBM is rarely curative, and tumors will recur in essentially all individuals.

Progression was defined in the EF-14 trial (Stupp et al [2015, 2017]) according to the MacDonald criteria (tumor growth >25% compared with the smallest tumor area measured in the individual during the trial or appearance of 1 or more new tumors in the brain that are diagnosed radiologically as glioblastoma multiforme).

U.S. Food and Drug Administration (FDA) approved devices that are used for the treatment of GBM include, *but are not limited to*:

- NovoTTF-100A™ System (Novocure; assigned the generic name of TTF)
- NovoTTF-200T System
- Optune®
- Optune System (NovoTTF-200A System)
- Optune Lua™ System (NovoTTF™-100L System)

To date, all of the existing tumor treating fields products fall under the brand name Optune. In March 2020, the manufacturer of Optune products announced a plan to include a suffix after the brand name for newly approved indications to further delineate specific indications for individual products (e.g., Optune Lua). Optune was renamed Optune Gio™ in 2023.

The FDA label includes the following notices:

- Individuals should use Optune for at least 18 hours a day to get the best response to treatment.
- Individuals should finish at least 4 full weeks of therapy to get the best response to treatment. Stopping treatment before 4 weeks lowers the chances of a response to treatment.

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Criteria:

- Tumor treating fields therapy to treat glioblastoma multiforme as an adjunct to standard maintenance therapy with temozolomide in individuals with newly diagnosed glioblastoma multiforme following initial treatment with surgery, radiotherapy, and/or chemotherapy is considered ***medically necessary*** with documentation of **ALL** of the following:

  1. Adult individuals ≥18 years of age
  2. Supratentorial tumor
  3. Karnofsky Performance Status score ≥70%
  4. Individual understands device use, including the requirement for a shaved head, and is willing to comply with use criteria according to the U.S. Food and Drug Administration label

- Tumor treating fields therapy for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

  - As an adjunct to standard medical therapy (e.g., bevacizumab, chemotherapy) for individuals with progressive or recurrent glioblastoma multiforme
  - As an alternative to standard medical therapy for individuals 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 individuals with malignant pleural mesothelioma

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Resources:

Literature reviewed 09/03/24. We do not include marketing materials, poster boards and non-published literature in our review.

Resources prior to 09/03/24 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. Ceresoli GL, Aerts JG, Dziadziuszko R, et al. Tumour Treating Fields in combination with pemetrexed and cisplatin or carboplatin as first-line treatment for unresectable malignant pleural mesothelioma (STELLAR): a multicentre, single-arm phase 2 trial. *Lancet Oncol*. Dec 2019;20(12):1702-1709. doi:10.1016/s1470-2045(19)30532-7

2. Davies AM, Weinberg U, Palti Y. Tumor treating fields: a new frontier in cancer therapy. *Ann N Y Acad Sci*. Jul 2013;1291:86-95. doi:10.1111/nyas.12112

3. FDA Grants Breakthrough Device Designation to the NovoTTF-200T System for Advanced Liver Cancer. September 9, 2021. Accessed May 11, 2024. https://www.novocure.com/fda-grants-breakthrough-device-designation-to-the-novottf-200t-system-for-advanced-liver-cancer/

4. 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*. Jun 2022;158(2):225-253. doi:10.1007/s11060-021-03900-w

5. Kanner AA, Wong ET, Villano JL, Ram Z. Post Hoc analyses of intention-to-treat population in phase III comparison of NovoTTF-100A™ system versus best physician's choice chemotherapy. *Semin Oncol*. Oct 2014;41 Suppl 6:S25-34. doi:10.1053/j.seminoncol.2014.09.008

6. Kesari S, Ram Z. Tumor-treating fields plus chemotherapy versus chemotherapy alone for glioblastoma at first recurrence: a post hoc analysis of the EF-14 trial. *CNS Oncol*. Jul 2017;6(3):185-193. doi:10.2217/cns-2016-0049

7. Kutuk T, Appel H, Avendano MC, et al. Feasibility of Tumor Treating Fields with Pemetrexed and Platinum-Based Chemotherapy for Unresectable Malignant Pleural Mesothelioma: Single-Center, Real-World Data. *Cancers (Basel)*. Apr 16 2022;14(8)doi:10.3390/cancers14082020

8. Mrugala MM, Engelhard HH, Dinh Tran D, et al. Clinical practice experience with NovoTTF-100A™ system for glioblastoma: The Patient Registry Dataset (PRiDe). *Semin Oncol*. Oct 2014;41 Suppl 6:S4-s13. doi:10.1053/j.seminoncol.2014.09.010

9. National Brain Tumor Society. Glioblastoma Facts & Figures. Accessed May 15, 2024. https://braintumor.org/take-action/about-gbm/

10. National Cancer Institute (NCI). Adult Central Nervous System Tumors Treatment (PDQ) Health Professional Version. Updated March 6, 2024. Accessed May 10, 2024. https://www.cancer.gov/types/brain/hp/adult-brain-treatment-pdq#cit/section_1.1

11. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Cancers. Version 1.2023. Accessed May 11, 2024. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf

12. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Mesothelioma: Pleural. Version 1.2024. Accessed May 12, 2024. https://www.nccn.org/professionals/physician_gls/pdf/meso_pleural.pdf

13. Novocure. Novocure announces Optune Lua as the brand name for the NovoTTF-100L system. March 19, 2020. Accessed May 11, 2024. https://www.novocure.com/novocure-announces-optune-lua-as-the-brand-name-for-the-novottf-100l-system/

14. Novocure. Novocure Announces Presentations on Tumor Treating Fields Therapy, Including New Clinical Data and Real-World Evidence, at 2023 Society for Neuro-Oncology Annual Meeting. Updated November 10, 2023. Accessed May 16, 2024. https://www.novocure.com/novocure-announces-presentations-on-tumor-treating-fields-therapy-including-new-clinical-data-and-real-world-evidence-at-2023-society-for-neuro-oncology-annual-meeting

15. Pless M, Weinberg U. Tumor treating fields: concept, evidence and future. *Expert Opin Investig Drugs*. Aug 2011;20(8):1099-106. doi:10.1517/13543784.2011.583236

16. Regev O, Merkin V, Blumenthal DT, Melamed I, Kaisman-Elbaz T. Tumor-Treating Fields for the treatment of glioblastoma: a systematic review and meta-analysis. *Neurooncol Pract*. Aug 2021;8(4):426-440. doi:10.1093/nop/npab026

17. 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*. Dec 19 2017;318(23):2306-2316. doi:10.1001/jama.2017.18718

18. Stupp R, Taillibert S, Kanner AA, et al. Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma: A Randomized Clinical Trial. *Jama*. Dec 15 2015;314(23):2535-43. doi:10.1001/jama.2015.16669

19. Stupp R, Wong ET, Kanner AA, et al. NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: a randomised phase III trial of a novel treatment modality. *Eur J Cancer*. Sep 2012;48(14):2192-202. doi:10.1016/j.ejca.2012.04.011

20. U.S. Food and Drug Administration (FDA). NovoTTF 100L System: Summary of Safety and Probable Benefit. May 23, 2019. Accessed May 12, 2024. https://www.accessdata.fda.gov/cdrh_docs/pdf18/H180002B.pdf

21. U.S. Food and Drug Administration (FDA). Tumor treatment fields. NovoTTF-10A System. Summary of safety and effectiveness data (SSED). Premarket Approval Application (PMA) No. P100034. 2011. Accessed May 11, 2024. http://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034b.pdf

22. U.S. Food and Drug Administration (FDA). Supplemental application for device name change. 2014. Accessed May 13, 2024. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_template.cfm?id=p100034s010

23. U.S. Food and Drug Administration (FDA). Summary of Safety and Effectiveness Data (SSED): OptuneTM (formerly NovoTTF-100ATM System). 2015. Accessed May 10, 2024. https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034S013B.pdf

24. Wong ET, Lok E, Swanson KD, et al. Response assessment of NovoTTF-100A versus best physician's choice chemotherapy in recurrent glioblastoma. *Cancer Med*. Jun 2014;3(3):592-602. doi:10.1002/cam4.210

25. Zhu JJ, Goldlust SA, Kleinberg LR, Honnorat J, Oberheim Bush NA, Ram Z. Tumor Treating Fields (TTFields) therapy vs physicians' choice standard-of-care treatment in patients with recurrent glioblastoma: a post-approval registry study (EF-19). *Discov Oncol*. Oct 14 2022;13(1):105. doi:10.1007/s12672-022-00555-5

Coding:

CPT: 77399
HCPCS: A4555, E0766, E1399

History:	Date:	Activity:
Medical Policy Panel	09/03/24	Review with revisions
Medical Director (Dr. Raja, Dr. Sutanto)	08/01/24	Review with no revisions
Medical Policy Panel	09/21/23	Review with revisions
Medical Policy Panel	08/01/23	Review with no revisions
Medical Policy Panel	08/16/22	Approved guideline (Effective 09/19/22)

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Policy Revisions:

09/03/24	Updated:	Description section; Resource section
09/21/23	Added:	"Insufficient evidence to support improvement of the net health outcome; or", and "Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, or" to experimental or investigational criteria bullets
09/21/23	Revised:	"Insufficient evidence to support improvement outside the investigational setting" from #3 to #5 in experimental or investigational criteria bullets
09/21/23	Updated:	Resource section

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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nílínigíí Blue Cross Blue Shield of Arizona haada yit'éego bína'ídíłkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yína'ídíłkidgo beehaz'áanii hóló díí t'áá hazaadk'ehjí háká a'doowołgo bee haz'ą doo bąąh íłínígóó. Ata' halne'ígíí kojį' bich'į' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون اية تكلفة. للتحدث مع مترجم اتصل ب 877-475-4799.

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Multi-Language Interpreter Services:

Tagalog: Kung ikaw, o ang iyong tinutulangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:
اگر شما، یا کسی که شما به او کمک میکنید ، سوال در مورد Blue Cross Blue Shield of Arizona ، داشته باشید حق این را دارید که کمک و اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799 [تماس حاصل نمایید.

Assyrian:
[illegible] Blue Cross Blue Shield of Arizona [illegible] 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคณ หรอคนทคณกาลงชวยเหลอมคาถามเกยวกบ Blue Cross Blue Shield of Arizona คณมสทธทจะไดรบความชวยเหลอและขอมลในภาษา ของคณไดโดยไมมคาใชจาย พดคยกบลาม โทร 877-475-4799