Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
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Plan: AmeriHealth Caritas Pennsylvania Community Health Choices	**Submission Date**: 8/1/2024
Policy Number: ccp.1111	**Effective Date:** 9/2014 **Revision Date:** July 1, 2024
Policy Name: Laser interstitial thermal therapy for drug-resistant epilepsy	

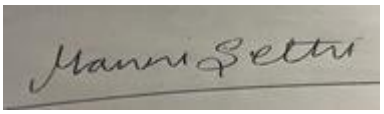
Type of Submission – Check all that apply:

- [ ] **New Policy**
- [x] **Revised Policy***
- [ ] **Annual Review – No Revisions**
- [ ] **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

See tracked changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Laser interstitial thermal therapy for drug-resistant epilepsy

Clinical Policy ID: CCP.1111

Recent review date: 7/2024

Next review date: 11/2025

Policy contains: Drug-resistant epilepsy; laser interstitial thermal therapy; laser thermal ablation; LITT; magnetic resonance imaging-guided laser thermal ablation.

AmeriHealth Caritas Pennsylvania Community HealthChoices has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania Community HealthChoices on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania Community HealthChoices will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are not guarantees of payment.

Coverage policy

Laser interstitial thermal therapy is clinically proven and, therefore, may be medically necessary for treatment of drug-resistant epileptic seizures, when all of the following criteria are met (Chen, 2023; Kohlhase, 2021; Wu, 2021):

- Failure to respond to, or intolerance of, at least two appropriately dosed antiepileptic medications to control disabling seizures.
- No contraindications to magnetic resonance imaging.
- Documentation of well-defined epileptogenic foci or critical pathways of seizure propagation accessible by laser interstitial thermal therapy.

Limitations

Contraindications include (Wu, 2021):

- Inability to identify the epileptogenic focus (or foci) or critical pathways within epileptogenic networks.
- Inability to undergo magnetic resonance imaging because of medical reasons.
- Medical contraindications to surgery, for example, unstable cardiac or respiratory conditions, anticoagulants that cannot be stopped, or bleeding diatheses.

Alternative covered services

Open surgical resection for epileptic seizures.

Background

A seizure is a temporary disturbance in brain function caused by excessive or abnormal signals in groups of neurons in the brain. Seizures may produce changes in awareness or sensation, involuntary movements, or other changes in behavior. Usually, a seizure lasts from a few seconds to a few minutes. Epilepsy, sometimes referred to as "*seizure disorder,"* is a general term that refers to a tendency to have recurrent seizures. An estimated three million adults and 456,000 children in the United States have epilepsy. New cases of epilepsy are most common among children and older adults (Centers for Disease Control and Prevention, 2024a).

Causes of epilepsy may be related to hereditary factors, early exposures, and events. Less than half of newly diagnosed cases have no known cause. Known conditions and events that may lead to epilepsy include (Centers for Disease Control and Prevention, 2024a):

- Cysticercosis infection.
- Oxygen deprivation (e.g., during childbirth).
- Traumatic brain injury or head injury.
- Stroke (resulting from a block or rupture of a blood vessel in the brain).
- Other neurologic diseases (e.g., Alzheimer's disease).
- Brain tumors.
- Certain genetic disorders.

Epileptic seizures are categorized broadly as generalized or partial seizures. Primary generalized seizures are seizures that begin with widespread involvement of both sides of the brain, whereas partial seizures begin with involvement of a smaller, localized area of the brain. With some partial seizures, the disturbance can still spread within seconds or minutes to involve widespread areas of the brain — causing a secondary generalized seizure (Centers for Disease Control and Prevention, 2024c).

Antiepileptic drug therapy is the treatment of choice for people with epilepsy. For approximately two-thirds of people with a correct diagnosis of epilepsy receiving optimum treatment, antiepileptic drugs are successful in fully controlling seizures. For those with drug-resistant epilepsy, other treatment options include epilepsy surgery, vagus nerve stimulation, and dietary therapies. The goal of surgery is to remove the smallest amount of tissue in order to achieve a seizure-free outcome. Epilepsy surgery is performed most often for seizure foci located in the temporal lobe (Centers for Disease Control and Prevention, 2024b).

Laser interstitial thermal therapy is a minimally invasive, surgical technique that uses magnetic resonance imaging to assess and guide focused laser energy to destroy the desired tissue. Surgeons make a three- to four-millimeter incision in the skull through which an intracranial probe is inserted and guided to the target; thermal ablation can be visualized in real time (Tariq, 2024).

This procedure is also called laser-induced interstitial thermotherapy, laser-induced thermotherapy, interstitial laser therapy, and laser ablation. Theoretically, critical adjacent tissue can be spared and open resection can be performed in the event ablation is ineffective. Laser interstitial thermal therapy may be an alternative to surgical resection for the treatment of focal lesional epilepsy in patients who are considered high-risk surgical candidates.

The U.S. Food and Drug Administration approved the Visualase thermal ablation system (Medtronic Navigation Inc., Louisville, Colorado) in 2006, and the NeuroBlate laser ablation system (Monteris Medical, Inc., Winnipeg,

California) in 2013. Both assist in identifying the target tissue under magnetic resonance imaging guidance while the laser is situated for precise ablation (U.S. Food and Drug Administration, 2006, 2013).

In 2018, the U.S. Food and Drug Administration issued recalls for the NeuroBlate and Visualase systems due to an unanticipated interaction between the thermal therapy system and magnetic resonance imaging causing inaccurate magnetic resonance thermometry during the procedure and potential injury to surrounding tissue. The Administration terminated the recall of Visualase in 2022 and of NeuroBlate in 2021 (U.S. Food and Drug Administration, 2024a, 2024b).

Findings

Guidelines

A guideline on laser interstitial thermal therapy for drug-resistant epilepsy cites evidence of “serious but well-recognised safety concerns” and the limited evidence on efficacy. The guideline recommends the procedure should only be used with special arrangements for clinical governance, consent, and audit or research (National Institute for Health and Care Excellence, 2020b).

The American Society for Stereotactic and Functional Neurosurgery position statement recommends magnetic resonance-guided laser interstitial thermal therapy for patients with drug-resistant epilepsy who: 1) fail to respond to, or are intolerant to, at least two appropriately chosen antiepileptic medications at appropriate doses, and 2) have well-defined epileptogenic foci or critical pathways of seizure propagation accessible by the procedure. Evidence from large case series demonstrated safety and efficacy of magnetic resonance-guided laser interstitial thermal therapy in reducing seizure frequency that was nearly comparable to data obtained from cases series of open surgical procedures. Longer-term outcome data are needed, but they should be weighed against the other benefits of a minimally invasive option such as shorter hospital stays, less surgical and neurological morbidity, and the ability to access deep or difficult-to-access targets (Wu, 2021).

Neither the American Academy of Neurology (undated) nor the American Epilepsy Society (undated) address laser interstitial thermal therapy in their evidence-based guidelines or practice parameters.

Evidence reviews

The evidence for laser interstitial thermal therapy consists of retrospective and prospective nonrandomized studies. Short follow up periods, small sample sizes, and inconsistent reporting of complications, particularly those affecting neurological outcomes, limit the ability to assess its relative safety, durability, and overall effectiveness as a first-line surgical option for patients with drug-resistant, medically-intractable temporal lobe epilepsy with different disease etiologies (National Institute for Health and Care Excellence, 2020a; Williams, 2019).

Compared to open surgical resection, laser interstitial thermal therapy is a safe procedure, is less effective for achieving freedom from seizures (Engel class I outcomes), and is associated with fewer postoperative neurological deficits ((Grewal, 2019; Kohlhase, 2021; Wang, 2020). Laser interstitial thermal therapy appears comparable to stereotactic radiosurgery, but superior to radiofrequency ablation, for reducing seizures with fewer adverse events, lower complication rates, and similar reoperation rates (Grewal, 2019; Kohlhase, 2021; National Institute for Health and Care Excellence, 2020a; Williams, 2019). Neurological deficits are largely transient. Approximately 15% required revision epilepsy surgery after the index procedure (Chen, 2023). Laser interstitial thermal therapy may be more appealing to select adult and pediatric patients with accessible, focal temporal lobe lesions who may be willing to accept lower efficacy in exchange for potentially better cognitive outcomes and quality of life.

A systematic review/meta-analysis of 26 studies (n = 804) compared treatment of drug-resistant epilepsy using minimally invasive procedures — laser interstitial thermal therapy or stereoelectroencephalography-guided radiofrequency thermocoagulation. Laser interstitial thermal therapy had a greater overall rate of freedom from seizures (65% versus 23%), but rates varied by etiology of epilepsy. Authors conclude both treatments are safe, and laser interstitial thermal therapy had a higher rate of post-operative freedom from seizures (Wang, 2020).

A systematic review and meta-analysis of 19 articles (n = 415) compared outcomes for persons with medically intractable temporal lobe epilepsy given either magnetic resonance-guided laser interstitial thermal therapy (n = 250) or stereotactic radiosurgery (n = 165). Insignificant differences between the two groups were observed for overall seizure freedom rate (*P* = .39), and seizure freedom rate for patients with lesional pathologic conditions (*P* = .23). The thermal therapy group had a lower complication rate (*P* = .06), but reoperation rates were similar (*P* = .31) (Grewal, 2019).

A meta-analysis of 16 studies (n = 269) assessed patients with drug-resistant epilepsy treated by laser interstitial thermal therapy guided by magnetic resonance imaging. The post-treatment prevalence of Engel Class I (least severe) patients was 61%, followed by 12%, 16%, and 15% for Classes II, III, and IV, respectively. Prevalence of post-operative complications was 24%. Authors conclude that this treatment is safe and effective for persons with treatment-resistant epilepsy (Xue, 2018).

Pediatric patients with epilepsy may also be candidates for this new therapy, although studies typically are limited by small numbers of subjects and short follow up periods. A randomized trial that compared pediatric patients (average age 10.3 years) with drug-resistant epilepsy who underwent open insular resection (n = 12) or laser interstitial thermal therapy (n = 14) followed subjects for an average of 2.43 years. The percent of Engel Class I (seizure free) in each group were relatively similar (50% versus 43%), and complications in both groups were minimal and mostly transient (Hale, 2019).

A systematic review/meta-analysis of 43 studies (n = 3,507) compared magnetic resonance-guided laser interstitial thermal therapy with other treatments for drug-resistant epilepsy. Interstitial laser thermal therapy achieved Engel Class I outcomes in 57% of patients versus 44% (radiofrequency ablation), 69% (anterior lobe resection), and 66% (selective amygdalohippocampectomy). Interstitial laser thermal therapy had comparable seizure outcomes versus radiofrequency ablation and inferior outcomes compared with the other two. Interstitial laser therapy had a similar complication rate compared to radiofrequency ablation, and fewer major complications versus the other two (Kohlhase, 2021).

In 2022, we added four systematic reviews/meta-analyses to the policy: Barot (2022, 28 studies, n = 559); Marathe (2021, 11 studies); Wang (2021, 19 studies); Zeller (2021, 35 studies, n = 303 pediatric procedures). We added one guideline (Wu, 2021). The new information from the analyses confirms the previous findings that laser interstitial thermal therapy is slightly less effective than open surgery for achieving seizure freedom in the short term, and stereotactic radiosurgery and radiofrequency ablation were the least effective options. Long term efficacy data are lacking, and neurological and neuropsychological outcomes are reported inconsistently.

In 2023, we added a new systematic review/meta-analysis (Chen, 2023) to the policy. We modified the medical necessity criteria to reflect the growing literature supporting a clinical benefit of laser interstitial thermal therapy as a minimally invasive alternative to open surgery for patients with focal drug-resistant epilepsy.

A systematic review and individual participant data meta-analysis included 46 studies (n = 450) with a median postoperative seizure freedom of 15.5 months and median follow-up duration of 19.0 months. The majority (69.7%) experienced seizure onset in childhood, and 67% of participants were adults at initial laser interstitial thermal therapy (mean age 29.5 ± 18.1 years). Unilateral procedures were evenly distributed between both hemispheres (53.2% left). Most procedures targeted the mesial temporal lobe (46.1%) or hypothalamus (15.1%).

In 113 participants, non-temporal neocortical targets included the insula (10.7%), frontal (8.2%), parietal (3.7%), and occipital (1.8%) lobes (Chen, 2023).

Complications occurred in 8.5% of participants, hemorrhage being the most common (5.2%). Postoperative neurological deficits occurred in 53 (15.1%), and most were transient (10.6%). The mean length of follow-up was 22.0 ± 13.7 months. At last follow up, 240 (57.8%) of 415 participants with refractory mesial temporal lobe epilepsy were seizure free. A total of 49 of 338 participants (14.5%) underwent revision epilepsy surgery after the index procedure. Hypothalamic hamartoma etiology and invasive electroencephalographic monitoring were independent predictors of post-operative neurological deficit. Independent predictors of seizure freedom were cerebral cavernous malformation and mesial temporal sclerosis/atrophy, while generalized seizure semiology and non-lesional findings on magnetic resonance imaging independently predicted faster time-to-seizure recurrence (Chen, 2023).

In 2024, we deleted several references and added two updated systematic reviews and meta-analyses (Alomar, 2023; Brenner, 2024) to the policy with no policy changes warranted. The results of the two analyzes highlight the challenge in quantifying functional and neurocognitive outcomes following laser interstitial thermal therapy. Data on these outcomes are limited, and data collection is heterogeneous. Alomar (2023; n = 836) reported an overall complication rate of 19.8%, with observed declines in verbal memory (24.2%), visual memory (25.2%), and naming (13.4%). The rate of visual field deficit was 7.8%, and the median follow-up period was 21.3 ± 10.42 months. Brenner (2024; n = 408) reported rates of decline in verbal cognition (20.4%) and visual cognition (13.5%), and variable rates of decline in other functional outcomes (cognitive emotion, visual deficits, attention/processing, motor cognition, and general executive function), ranging from 10.5% to 25%. Both study groups call for standardized reporting to better capture procedure risk that impact quality of life.

References

On May 29, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “interstitial laser therapy,” “laser interstitial thermal therapy,” “laser induced ablation,” “laser thermal ablation,” “laser induced thermotherapy,” “NeuroBlate,” “visualase,” and “epilepsy.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

6/2014: initial review date and clinical policy effective date: 9/2014

6/2019: Policy references updated. Policy number changed to CCP.1111.

6/2020: Policy references updated.

6/2021: Policy references updated.

6/2022: Policy references updated.

6/2023: Policy references updated. Coverage modified.

6/2024: Policy references updated.