08.01.37 External Upper Limb Stimulation for the Treatment of Tremors

Original Effective Date: November 2022

Review Date: December 2025

Revised: December 2024

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Related Policies:

- 01.01.33 Cranial Electrotherapy Stimulation and Auricular Electrostimulation
- 01.01.34 Interferential Current Stimulation

Summary

Description

Essential tremor (ET) is the most common neurological disorder among adults and is the most prevalent tremor disorder. Individuals with Parkinson Disease (PD) may also have action tremors in the hands or arms that impair activities of daily living. There is no cure for ET or PD and only a handful of pharmacologic or surgical treatments exist to help individuals manage their symptoms. An external upper

limb tremor stimulation device (transcutaneous afferent patterned stimulation [TAPS]) is being evaluated as a method to reduce tremor in individuals with ET and PD. In addition to more traditional settings such as a physician's office or an outpatient clinic, these techniques can be self-administered in an individual's home.

Summary of Evidence

For individuals who have ET who receive transcutaneous afferent patterned stimulation (TAPS), the evidence includes a pragmatic randomized controlled trial (RCT), a nonrandomized, prospective study, and a retrospective database study. Relevant outcomes are symptoms, functional outcomes, quality of life (QOL) and medication use. Although the RCT indicated reduced tremor power among patients receiving TAPS, the trial lacked thorough analysis of clinically relevant outcomes, was open-label, and short-term. Results from the nonrandomized study suggest that TAPS therapy is effective and safe for patients with essential tremor. However, the trial was limited by its open-label, single-arm design, lack of defined standards for what constitutes a clinically meaningful improvement in stated endpoints, and exclusion of patients who exited the study early from the pre-specified primary and secondary endpoint analyses. Further studies comparing TAPS to standard of care therapy for essential tremor are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have action tremor associated with PD who receive TAPS, the evidence includes a prospective, open-label, single-arm study. Relevant outcomes are symptoms, functional outcomes, QOL, and medication use. Results of the prospective trial suggest that repeated in-home TAPS therapy is effective for reducing tremor power and safe for patients with essential tremor. Limitations identified were the open-label, single-arm design, and lack of long-term outcomes. Further studies comparing TAPS to pharmacologic therapy for tremor associated with Parkinson disease are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information

Not applicable.

OBJECTIVE

The objective of this evidence review is to evaluate if external upper limb tremor stimulation devices transcutaneous afferent pattered stimulation improve the net health outcome for individuals with essential tremor and action tremor due to Parkinson disease.

PRIOR APPROVAL

Not applicable.

POLICY

Transcutaneous afferent patterned stimulation (TAPS) is considered **investigational** for all indications, including but not limited to the following, because the evidence is insufficient to determine the effects of the technology on net health outcomes:

- Essential tremor (ET)
- Action tremor for Parkinson disease

POLICY GUIDELINES

Coding

See the Codes table for details.

BACKGROUND

Essential tremor (ET) is characterized as movement that is rhythmic and involuntary, most commonly in the hand and/or arms. ET is the most common neurological disorder among adults and is the most prevalent tremor disorder. The exact mechanisms of ET are not fully understood, however recent studies suggest that ET may be a neurodegenerative disorder.

Parkinson disease is a neurodegenerative motor disorder associated with a loss of dopamine-producing cells in the brain. Parkinson disease is characterized by both rigidity of movement and tremors of the extremities.

There is no cure for ET or Parkison disease and only a handful of pharmacologic or surgical treatments exist to help individuals manage their symptoms. First-line treatment consists of pharmacotherapies, such as propranolol and primidone. Second and third-line pharmacological approaches include topiramate, gabapentin, other beta-blockers, or benzodiazepines. However, response to pharmacotherapies varies, and high doses are often required for effective tremor reduction, increasing the burden of side effects for individuals, and reducing tolerability and compliance. Deep brain stimulation surgery and magnetic resonance imaging (MRI)-guided focused ultrasound ablation are additional treatment options for tremor. However, not all individuals are appropriate candidates for such surgical procedures.

External upper limb tremor stimulation device (Cala Trio and Cala kIQ [Cala Health, Inc. Burlingame, CA]), is an on-demand, non-invasive, wrist-worn device that delivers individualized electrical stimulation to the nerves of the arm in people with ET or PD, such as is delivered by Cala-Therapy. The proposed action of this device is the delivery of transcutaneous afferent patterned stimulation (TAPS) to the ventral intermediate nucleus thalamus, a key relay point in the central tremor network, and one target of deep brain stimulation (DBS), an invasive treatment of ET. Noninvasive TAPS stimulation to the upper limb using the Cala device is calibrated to an individual's tremor pattern and the user can adjust its strength to account for daily variations in tremor activity.

Regulatory Status

In October 2021, the U.S. Food and Drug Administration (FDA) granted 510k clearance for Cala Trio Therapy with the indication to aid in the temporary relief of hand tremors in the treated hand following stimulation in adults with ET. The device stimulates the nerves in the arm to disrupt the neural signals that cause essential tremor. The predicate device to the Cala Trio was the CalaONE, which obtained De Novo designation from the FDA in May 2017 (DEN170028). According to the De Novo summary document, the CalaONE failed to show a benefit versus placebo (FDA, 2017).

The Cala kIQ™ (Cala Health) received FDA 510(k) marketing clearance in November 2022 (K222237). The Cala kIQ is indicated for temporary relief of postural and kinetic tremor symptoms that impact some activities of daily living in adult patients with PD in addition to hand tremors in adults with ET. Prior submissions were listed as DEN170028, K182706, and the predicate K203288.

Cala Trio and Cala kIQ use transcutaneous afferent patterned stimulation (TAPS) therapy which consists of bursts of non-invasive electrical stimulation applied to the median and radial nerves.

RATIONALE

This evidence review was created in November 2022 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through December 2025.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to individuals and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Essential Tremor

Clinical Context and Therapy Purpose

The purpose of transcutaneous afferent patterned stimulation (TAPS) is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with essential tremor (ET).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with ET.

Interventions

The therapy being considered is TAPS. TAPS provides stimulation that alternates between the median and radial nerves with calibration to tremor frequency.

Comparators

The following therapies are currently being used to manage ET: pharmacotherapy.

Outcomes

The general outcomes of interest are reductions in symptoms and medication use and improvements in functional outcomes and QOL.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded

Review of Evidence

Systematic Review

Hayes Evolving Evidence Review January 2024 of Cala Trio for treatment of essential tremor found poor quality evidence (1 poor quality RCT and 1 poor quality pretest-posttest study) and additional studies are needed to determine whether this device provides incremental benefit over pharmacotherapy or whether its performance is worse, the same or better than alternative adjunctive treatments. Also, while this device may be perceived as an alternative to pharmacotherapy with lower incidence of adverse events, many patients identified in the studies used it as an adjunctive treatment to pharmacotherapy and many patients (4% and 18% per study) experienced nonserious cutaneous side effects.

Randomized Controlled Trials

Dai et al (2023) conducted a pragmatic RCT in which adult patients with essential tremor were selected from an insurance database and randomized to a wrist-worn, US Food and Drug Administration (FDA)-approved, TAPS device (Cala Trio) plus standard of care or standard of care alone for 1 month. Standard of care included a variety of medications with the majority of patients receiving propranolol or another beta-blocker. After 1 month, all enrolled patients were provided open-label treatment with TAPS. All enrolled patients had the device delivered to their home. Characteristics and results of the trial are summarized in Tables 1 and 2, respectively. The primary outcome of the trial was tremor power as measured by motion sensors in the device at 1 month. Tremor power is a calculation of amplitude and frequency. Tremor power decreases with lower amplitude and lower frequency motions. The majority of the patients were White (84.42%) and male (66.30%) with a mean age of 68.21 years. The trial is limited by the open-label design and the lack of reporting of long-term outcomes.

Table 1. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Dai et al (2023)	U.S.	NA	2021-2023	310 adults (≥22 years) with essential tremor	TAPS (n=158)	SOC (n=152)

NA: not applicable; RCT: randomized controlled trial; SOC: standard of care; TAPS: transcutaneous afferent patterned stimulation.

Table 2. Summary of Key RCT Results

Study	Tremor Power (geometric mean ± SD)	Change in BF-ADL
Dai et al (2023)	N=276	N=134
TAPS	0.017 $(m/s^2)^2$ ± 0.003	1.6
SOC	0.08 $(m/s^2)^2$ ± 0.014	0.2
Effect size	0.063	1.4
p-value	<.0001	.0187

BF-ADL: Bain & Findley Activities of Daily Living; RCT: randomized controlled trial;
SD: standard deviation; SOC: standard of care; TAPS: transcutaneous afferent patterned stimulation.

Nonrandomized Studies

Isaacson et al (2020) evaluated the repeated home use of an FDA-cleared wrist-worn TAPS device in the Prospective Study for Symptomatic Relief of Essential Tremor with Cala Therapy (PROSPECT) trial. Key characteristics of the trial are summarized in Table 3. For each active treatment session, the device electrically stimulated the median and radial nerves for 40 minutes with an alternating burst pattern tuned to the frequency of each patient's tremor. The pre-specified co-primary endpoints were improvements on the clinician-rated Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) and patient-rated Bain & Findley Activities of Daily Living (BF-ADL) dominant hand scores. Of the 263 enrolled patients, 205 completed the visit 3 follow-up and were included in the primary analysis. Results revealed a significant improvement in TETRAS and BF-ADL from pre- to post-stimulation at each clinic visit (p<.0001 for all comparisons). Pre-stimulation tremor levels were improved from Visit 1 to 3 on both TETRAS and BF-ADL (p<.0001 for both). Patients rated as "severe" or moderate" improved with both TETRAS (49.3% at baseline to 21% at study exit) and BF-ADL (64.8% at baseline to 23% at study exit) scoring. Tremor power was also noted to significantly improve with therapy from pre- to post-stimulation (p<.0001). No device-related serious adverse events were reported. Non-serious device-related adverse events occurred in 18% of patients (e.g., persistent skin irritation, sore/lesion, discomfort, electrical burns, and minor skin irritation). Limitations identified were the open-label, single-arm design, the lack of consensus for the definition of clinically meaningful improvement in TETRAS or BF-ADL, as well as the exclusion of 58 patients who exited the study early from the pre-specified primary and secondary endpoint analyses.

Lu et al (2023) evaluated long-term outcomes with a TAPS device (Cala Trio) in patients (N=1223) with essential tremor from the manufacturer's database. Duration of usage ranged from 90 days to 1223 days with an average use of 5.6 TAPS sessions per week. The geometric mean tremor power improvement was 2.8, a 64.3% improvement in tremor power. Approximately half of the patients (49.8%) had at least 50% tremor reduction.

Table 3. Summary of Nonrandomized Trials

Study	Study Type	Country	Participants	Treatment	Follow-Up
Isaacson et al (2020)	Prospective, multicenter, single-arm, open-label	U.S. - 26 sites	263 patients (≥22 years) diagnosed with essential tremor having at least 1 dominant hand task scoring ≥2 on the clinician-rated TETRAS and ≥3 on the self-rated BF-ADL, and having a total score across all dominant hand tasks ≥6 on TETRAS and ≥8 on BF-ADL	Cala wrist-worn TAPS device; patients were instructed to use the device twice daily for 3 months	Three in-clinic visits: Visit 1 (patient screening and enrollment); Visit 2 (1 month follow-up); Visit 3 (3 month follow-up and study completion)
Lu et al 2023	Retrospective database	U.S.	1123 patients prescribed TAPS for essential tremor who had used TAPS for ≥90 days	Cala-Trio wrist-worn TAPS device	

BF-ADL: Bain & Findley Activities of Daily Living; TETRAS: Tremor Research Group Essential Tremor Rating Assessment Scale.

Section Summary: Essential Tremor

The evidence for the use of TAPS for essential tremor includes results from a single pragmatic RCT; a prospective, open-label, post-clearance, single-arm study; and a retrospective database study. Although the RCT indicated reduced tremor power among patients receiving TAPS, the trial lacked thorough analysis of more clinically relevant outcomes, was open-label, and short-term. Results of the prospective trial suggest that repeated in-home non-invasive TAPS therapy is effective and safe for individuals with essential tremor. Limitations identified were the open-label, single-arm design, the lack of consensus for the definition of clinically meaningful improvement in TETRAS or BF-ADL, as well as the exclusion of 58 individuals who exited the study early from the pre-specified primary and secondary endpoint analyses. Further studies comparing TAPS to pharmacologic therapy for essential tremor are needed.

Action Tremor in Parkinson Disease

Clinical Context and Therapy Purpose

The purpose of TAPS in individuals who have action tremor associated with Parkinson disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with an action tremor associated with Parkinson disease.

Interventions

The therapy being considered is TAPS. TAPS provides stimulation that alternates between the median and radial nerves with calibration to tremor frequency.

Comparators

The following therapies are currently being used to manage action tremor in Parkison disease: pharmacotherapy.

Outcomes

The general outcomes of interest are reductions in symptoms and medication use, and improvements in functional outcomes and QOL.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded

Review of Evidence

An industry-sponsored single-arm study of TAPS in patients with action tremor in Parkinson disease (PD) was reported by Brillman et al (2023). Forty patients with action tremor in PD who had impaired activities of daily living (ADL) as measured by a score $\geq$ 2 on the Movement Disorder Society-Unified Parkinson Disease Rating Scale (MDS-UPDRS) in the medication-off state were enrolled in the study. Exclusion criteria were numerous. Patients were treated with twice daily sessions of TAPS for 4 weeks with study visits before and after the 4 weeks of home use in the medication-off state. The primary outcome, change in tremor power measured by the device accelerometer before and immediately after a stimulation session, was reduced by 64% with 79% of patients showing at least 50% reduction. Additional endpoints, collected before the first session and immediately after the last stimulation session, were the change in the MDS-UPDRS, BF-ADL scale, and clinical global impression-improvement (CGI-I) and patient global impression-improvement (PGI-I). These showed statistically significant improvement when measured immediately after the last session, but durability of the treatment effect in minutes was assessed only by survey, with 78% of patients reporting a median 60-minute duration of post-stimulation relief in this single-arm study. Limitations of the study include having assessments immediately after stimulation, the subjective assessment of durability, and the lack of a control group or blinding. See Table 4 for study summary.

Table 4. Summary of Key Nonrandomized Trial

Study	Study Type	Country	Participants	Treatment	Follow-Up
Brillman et al (2023)	Prospective, single-center, single-arm, open-label	U.S.	40 patients diagnosed with PD and impaired ADL as measured by a score ≥2 on	Cala wrist-worn TAPS device; patients were instructed to use the	Two in-clinic visits: Visit 1

			the MDS-UPDRS in the medication-off state	device twice daily for 1 month	(training) Visit 2 (1 month follow-up)

ADL: activities of daily living; MDS-UPDRS: Movement Disorder Society Unified PD Rating Scale; PD: Parkinson disease; TAPS: transcutaneous afferent patterned stimulation.

Section Summary: Action Tremor Associated with Parkison Disease

The evidence for the use of TAPS for action tremor associated with PD includes results from a prospective, open-label, single-arm study. Results of the prospective trial suggest that repeated in-home TAPS therapy is effective for reducing tremor power and safe for individuals with essential tremor. Limitations identified were the open-label, single-arm design, and lack of long-term outcomes. Further studies comparing TAPS to pharmacologic therapy for tremor associated are needed.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Neurology (AAN)

In 2011, the American Academy of Neurology (AAN) updated the 2005 evidence-based guideline for the treatment of essential tremor (ET) that was last reaffirmed July 2022. This guideline includes recommendations for pharmacologic agents and surgical interventions for individuals with ET. No recommendations for use of transcutaneous afferent patterned stimulation (TAPS) as a treatment of ET are provided.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

REFERENCES

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
		None
HCPCS		
	E0734	External upper limb tremor stimulator of the peripheral nerves of the wrist
	A4542	Supplies and accessories for external upper limb tremor stimulator of the peripheral nerves of the wrist
Type of Service	Durable Medical Equipment	
Place of Service	Home Inpatient Outpatient	

POLICY HISTORY

Date	Action	Action
December 2025	Annual Review	Policy Renewed
November 2024	Annual Review	Policy Revised
November 2023	Annual Review	Policy Revised
November 2022		New Medical Policy Created

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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