# Experimental, Investigational, or Unproven

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## Introduction

Items currently considered to be experimental, investigational, or unproven in this guideline include but are not limited to the following:

- Distal Transcutaneous electrical nerve stimulator, stimulates peripheral nerves of the upper arm (HCPCS A4540)
- Neuromodulation stimulator system, adjunct to rehabilitation therapy regime (HCPCS A4593)
- Neuromodulation stimulator system, adjunct to rehabilitation therapy regime, mouthpiece each (HCPCS A4594)
- Cranial electrical stimulation (cranial electrotherapy stimulation) (HCPCS E0732, A4596)
- Trancutaneous tibial nerve stimulator (HCPCS E0736)
- Upper extremity rehabilitation system providing active assistance to facilitate muscle re-education, include microprocessor, all components and accessories (HCPCS E0738)
- Rehab system with interactive interface providing active assistance in rehabilitation therapy, includes all components and accessories, motors, microprocessors, sensors (HCPCS E0739)

## Criteria

### Experimental, Investigational, or Unproven

Certain studies, treatments, procedures, or devices may be considered experimental, investigational, or unproven for any condition, illness, disease, or injury being treated if one of the following is present:

- There is a paucity of supporting evidence.
- The evidence has not matured to exhibit improved health parameters.
- Clinical utility has not been demonstrated in any condition.
- The study, treatment, procedure, or device lacks a collective opinion of support.

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Supporting evidence includes standards that are based on credible scientific evidence published in peer-reviewed medical literature (such as well conducted randomized clinical trials or cohort studies with a sample size of sufficient statistical power) generally recognized by the relevant medical community. Collective opinion of support includes physician specialty society recommendations and the views of physicians practicing in relevant clinical areas when physician specialty society recommendations are not available.

## Codes addressed in this guideline

**Note:**

There may be additional items considered Experimental, Investigational, or Unproven. This list is not intended to be inclusive of all items.

| HCPCS | Description |
|---|---|
| A4540 | Distal transcutaneous electrical nerve stimulator, stimulates peripheral nerves of the upper arm |
| A4593 | Neuromodulation stimulator system, adjunct to rehabilitation therapy regime |
| A4594 | Neuromodulation stimulator system, adjunct to rehabilitation therapy regime, mouthpiece each |
| A4596 | Cranial electrotherapy stimulation (CES) system supplies and accessories, per month |
| E0732 | Cranial electrotherapy stimulation (CES) system, any type |
| E0736 | Transcutaneous tibial nerve stimulator |
| E0738 | Upper extremity rehabilitation system providing active assistance to facilitate muscle re-education, include microprocessor, all components and accessories |
| E0739 | Rehab system with interactive interface providing active assistance in rehabilitation therapy, includes all components and accessories, motors, microprocessors, sensors |

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## Evidence Discussion

### HCPCS A4540: Distal Transcutaneous electrical nerve stimulator, stimulates peripheral nerves of the upper arm

Definitions/Background (HCPCS A4540)

A Distal Transcutaneous electrical nerve stimulator, stimulates peripheral nerves of the upper arm (Remote electrical neuromodulation (REN) device) is used for the acute treatment of migraine. The mechanism of action involves electrical stimulation applied to peripheral nerves in the upper arm to induce conditioned pain modulation. The device is affixed to the individual's arm and is operated using a smartphone application.

Literature review (HCPCS A4540)

- Nerivio™ (Theranica Bio-Electronics Ltd., Israel) is a Food and Drug Administration's (FDA)-approved wireless REN device indicated for individuals 12 years of age or older for acute treatment of episodic or chronic migraine.
- According to the Medicare Benefit Category and Payment Determination for Nerivio™ (CMS, 2022), "Once used, the Nerivio™ can support 540 minutes of treatments, or 12 treatments of 45 minutes, but only up to an 18 month period. The Nerivio™ device can be used up to an 18 month period; therefore, the minimum lifetime requirement of three years is not met. According to the Nerivio™ user manual, when there are no more treatments left, the device should be disposed. DME is a benefit for rental of equipment for use in the home and therefore DME items must be able to withstand repeated use by successive patients in accordance with Medicare regulations and as indicated in Medicare program instructions at chapter 15, section 110.1 of the Medicare Benefit Policy Manual (CMS Pub. 100-02) and chapter 1, part 4, section 280.1 of the Medicare National Coverage Determinations Manual (CMS Pub. 100-03)."
- Yarnitsky et al. (2019) conducted a randomized controlled trial including 252 participants to examine the safety and efficacy of a REN device compared to a sham device for the acute treatment of migraine. A smartphone-controlled wireless REN device was applied for 30-45 minutes on the upper arm within one hour of migraine attack onset. Migraine pain levels and most bothersome symptoms (MBS) were recorded at baseline, two, and 48 hours post-treatment. The primary efficacy endpoint was the proportion of participants achieving pain relief at two hours post-treatment. Relief of MBS and absence of pain at two hours were key secondary endpoints. Participants receiving active stimulation achieved more pain relief, which was sustained 48 hours post-treatment. The incidence of device-related adverse events was low and similar between treatment groups. The authors concluded that REN is an effective acute migraine treatment with a favorable safety and tolerability profile. However, the authors noted several drawbacks to the study, including a low rate of

severe baseline pain intensity and high rate of mild pain intensity, a lack of reported efficacy of the device at intervention periods over one hour of symptom onset, and the difficulty of selecting an appropriate sham device for successful blinding.

- Tepper et al. (2023) conducted a randomized controlled trial including 179 individuals that evaluated the use of REN for the prevention of migraine. Participants used either a REN device or a sham device every other day for an eight week intervention period. Participants reported their symptoms daily via an electronic diary. REN was superior in the change in mean number of episodic and chronic migraine days per month from baseline, reduction of moderate/severe headache days, reduction of headache days, percentage of individuals achieving 50% reduction in moderate/severe headache days, and reduction in days of acute medication intake. No serious device-related adverse events were reported in any group. The authors concluded that when used every other day, REN is effective and safe for the prevention of migraine headache.
- An open-label, single arm study (Hershey et al., 2021) including 39 adolescents (ages 12–17 years old) evaluated the safety, tolerability, and efficacy of REN during an eight week treatment phase with a REN device. Pain severity, associated symptoms, and functional disability were recorded at treatment initiation, and two and 24 hours post-treatment. At two hours post treatment, pain relief was achieved by 71% (28/39) and pain free status was achieved by 35% (14/39). One device-related adverse event was reported in which a temporary feeling of pain in the arm was felt. The authors concluded that REN may offer a safe and effective non-pharmacologic alternative for acute treatment of migraine in adolescents. However, this study was limited by a lack of a placebo control group, small sample size, and high dropout rate.
- Grosberg et al. (2021) conducted an open-label, single arm study including 91 individuals to evaluate pain relief, improvement of symptoms, and functional disability during a four week trial using a REN device. Participants used an electronic diary to record symptoms at treatment initiation, two hours after treatment, and 24 hours after treatment. Pain relief and pain disappearance at two hours were achieved by 59.3% (54/91) and 20.9% (19/91), and sustained pain relief at 24 hours was observed in 64.4% (29/45) of those who achieved pain relief at two hours. One device-related adverse event was reported as mild pain in the arm after device use. The investigators concluded that REN may provide a non-pharmacological acute treatment option in individuals with chronic migraine. Of note, the authors reported several limitations to the study including: lack of a sham stimulation group, small number of subjects included in the study, and a reported nonadherence with study protocol. The authors noted that additional studies with a larger number of subjects are needed.
- An open-label, single arm study (Nierenburg et al., 2020) including 38 individuals with chronic migraine assessed the efficacy of a REN device over a four week treatment phase. At two hours, 73.7% (28/38) achieved pain relief and 26.3% (10/38) were pain-free. At 24 hours, 84.4% (27/32) had sustained pain relief response and 45.0% (9/20) had sustained pain relief response at 24 hours in at least 50% of their treated

attacks. The effects of REN on associated symptoms and improvement in function were also consistent. The incidence of device-related adverse events was low (1.8%). This adverse event included bilateral tingling in the temples and double vision. The authors concluded that REN may be an efficacious treatment option with a favorable safety profile for acute treatment of migraine in individuals with chronic migraine. However, the authors noted that the study has several limitations including lack of a placebo control group and a small sample size. The authors concluded that further studies with larger sample sizes are warranted.

**HCPCS A4593, A4594: Neuromodulation stimulator system, adjunct to rehabilitation therapy regime**

Definitions and Background (HCPCS A4593, A4594)

A neuromodulation stimulator system (i.e., Portable Neuromodulation Stimulator (PoNS®) (Helius Medical Inc.)) describes a translingual, non-implantable tongue stimulator intended for use as a short-term adjunct to a supervised therapeutic exercise program for the treatment of a gait deficit due to mild to moderate symptoms of multiple sclerosis (MS) in individuals 22 years of age and over. The device provides therapy through a controller and a mouth piece. The controller (HCPCS A4593) generates the delivery of electrotactile stimulation to the trigeminal and facial nerves through the mouthpiece (HCPCS A4594) while the individual is performing prescribed therapeutic exercises to directly activate brainstem areas and trigger neuroplastic changes in the brain (cerebral cortex) over a 14-week therapeutic period.

Literature Review (HCPCS A4593, A4594)

- PoNS® received the Food and Drug Administration's (FDA's) De Novo clearance in March 2021 (US FDA, 2021) indicated for use as a short-term treatment of gait deficit due to mild to moderate symptoms from MS.
- Tyler et al. (2014) conducted a randomized trial including 20 individuals with chronic MS and gait disturbance to examine the effect of targeted physical therapy with and without cranial nerve non-invasive neuromodulation (CN-NINM). The primary outcome measure was the Dynamic Gait Index (DGI) where the clinician scored an index of eight gait tasks. The DGI was assessed at baseline, two weeks, six weeks, 10 weeks, and 14 weeks. The results showed that the PoNS® group on average achieved improvement in their DGI score of 7.95 at the end of the study, which was statistically significant and clinically significant, compared to the control group. The authors concluded that tongue-based neurostimulation may amplify the benefits of exercise for improving gait in people with chronic MS. However, the investigators noted that the sample size was small, and further studies are warranted to determine the efficacy of this intervention.
- Boughen et al. (2022) conducted a systematic review of 40 studies including individuals with traumatic brain injury, multiple sclerosis, Parkinson's disease and

spinal cord injury who used cranial nerve noninvasive neuromodulation (CN-NINM) via translingual nerve stimulation (TLNS). Most studies used the PoNS® device in conjunction with a rehabilitation program to improve functional outcomes such as balance and gait. The authors concluded that the findings suggest that TLNS is a feasible modality that can be incorporated into home-based programs. However, further research on which populations, including clinical indicators, is indicated for TLNS and the optimal parameters are required.

**HCPCS E0732, A4596: Cranial electrotherapy stimulation (CES) system**

Definitions/Background (HCPCS E0732, A4596)

- Cranial electrotherapy stimulation (CES), also known as cranial electrical stimulation, transcranial electrical stimulation, or electrical stimulation therapy, is a non-invasive form of neurostimulation that uses a battery operated device to deliver low voltage, alternating current to the brain via electrodes attached to the scalp or infra- or supra-auricular structures (e.g., earlobes, mastoid processes, zygomatic arches, or maxilla-occipital junctions). CES has been evaluated for the treatment of a variety of conditions, including but not limited to anxiety, depression, insomnia, pain, fibromyalgia, and opiate withdrawal. The mechanism of action is thought to be the modulation of activity in brain networks by direct action in the hypothalamus, limbic system, and/or the reticular activating system.

Literature Review (HCPCS E0732, A4596)

- Cranial electrotherapy stimulation (CES) was brought to the US market in 1973 with the introduction of the Electrosone 50. This device was purported to induce sleep and relaxation. The Neurotone 101 was the first FDA-approved CES device. It was introduced in 1978 and was marketed for treatment of anxiety, depression, and insomnia (Brunyé et al., 2021). From their original introduction through the early 2000s, CES devices were regulated by the FDA as Class III devices. Class III devices require premarket approval and clinical efficacy and safety data submission. In 2014, the FDA reclassified CES devices marketed to treat anxiety or insomnia as Class II devices, which do not require premarket approval, but do require special controls to provide reasonable assurance of safety and effectiveness (US FDA, 2022). CES devices which are marketed to treat depression remain Class III devices.
- Per FDA regulations, CES devices should only be available to patients when prescribed by licensed medical practitioners (Brunyé et al., 2021). Some Class II CES devices available to treat anxiety and insomnia in the United States as of early 2024 include: Alpha-Stim® AID (Electromedical Products International, Inc.), Alpha-Stim® M (Electromedical Products International, Inc.), and CES Ultra (Neuro-Fitness, LLC).
- Shekelle et al. (2018) conducted a systematic review and identified three randomized controlled trials that compared active CES with sham CES in individuals with unipolar or bipolar depressive syndromes. The authors noted that the included trials had

small sample sizes and short durations. Thus, the authors concluded that evidence is insufficient to support the use of CES for indications including fibromyalgia, headache, musculoskeletal pain, degenerative joint pain, depression, or insomnia; low-strength evidence suggests modest benefit in individuals with anxiety and depression.

- A Cochrane review (Kavirajan et al. 2014) examined randomized controlled trials evaluating CES versus sham CES for the acute treatment of depressive disorder in adults. The authors concluded that there was a lack of high-quality studies of CES in treatment of acute depression. Moreover, the authors reported a need for additional double-blind randomized controlled trials of CES in the treatment of acute depression.
- A double-blind, sham controlled randomized trial (McClure et al., 2015) including 16 individuals evaluated the efficacy and safety of CES in the treatment of bipolar II depression. Participants were randomized into two treatment groups: active CES or sham stimulation. The 12-week study design included the following three stages: double-blind phase (weeks 1–2), open-label phase (weeks 3–4), and follow-up phase (weeks 5–12). Scores on a self-administered depression rating scale (Beck Depression Inventory) improved more with active than sham stimulation, but improvement on the clinician-administered scale (Hamilton Rating Scale for Depression) was comparable for the two groups. In addition, the incidence of adverse effects, including manic symptoms, did not differ between the two groups. The authors concluded that CES may be an effective and low-risk treatment for individuals with bipolar depression. However, the authors noted the study was limited by a small sample size and specific sub-population of bipolar II depressed individuals, which limits the generalizability of the findings.
- A randomized controlled trial (Gong et al., 2016) investigated the effect of CES combined with biofeedback therapy (BFT) on the psychological state, clinical symptoms, and anorectal function in individuals with functional constipation. The study included 74 individuals who were assigned to two groups: BFT (control) or CES combined with BFT (experimental). Participants were assessed using the self-rating anxiety scale (SAS), self-rating depression scale (SDS), Wexner constipation score, and anorectal manometry and balloon expulsion tests before and after treatment. After treatment, the participants in the combined CES and BFT group had significantly lower SAS, SDS, and Wexner constipation scores than the control group. In addition, the number of successful explusions was larger in the experimental group. The authors concluded that CES combined with BFT was effective in improving psychological symptoms (anxiety and depression) and bowel symptoms in individuals with functional constipation. However, the authors reported several limitations including: anorectal manometry was not performed in all participants thus affecting an outcome measure, the sample size was small, the study lacked long-term follow-up, the trial was unblinded, and most outcomes were self-reported. The authors suggested that future research is warranted with long-term follow-up, prospective studies, and larger sample sizes.

- Chung et al. (2023) performed a meta-analysis including eight randomized controlled trials and 337 individuals to examine the therapeutic effects of CES in individuals with anxiety, depressive, and insomnia symptoms. The authors concluded that the therapeutic effectiveness of CES for symptoms of anxiety, depression, and insomnia in individuals with anxiety using the Alpha Stim® device was better in the CES group than in the control group. However, the authors acknowledged the need for more large-scale, well-controlled clinical investigations, as they noted that most studies used sham devices with a short-term duration.
- Lee et al. (2023) conducted a randomized controlled study including 62 individuals with depression to investigate the effectiveness of CES in reducing stress. The intervention group used the device for 30 minutes twice a day for three weeks. After the intervention, the depression rating scales (measured via the Beck depression inventory-II) significantly improved in the CES group compared to the sham group. In addition, the stress response (measured by quantitative electroencephalography (QEEG) and serial salivary cortisol levels) significantly improved in the CES group compared to the sham group. Thus, the investigators concluded that CES may alleviate depressive symptoms and stress response; however, the authors noted that bias may have been introduced during the process because device use and sample collection were self-conducted by participants at home.

**HCPCS E0736: Transcutaneous Tibial Nerve Stimulator**

Definitions/Background (HCPCS E0736)

A Transcutaneous tibial nerve stimulator (TTNS) is a device designed to deliver non-invasive transcutaneous electrical stimulation of the posterior tibial nerve. The device is used for the treatment of overactive bladder (OAB) and the associated symptoms of urinary urgency, urinary frequency, and urge incontinence.

Literature Review (HCPCS E0736)

- Percutaneous tibial nerve stimulation (PTNS) can be used to treat overactive bladder (OAB) and fecal incontinence. PTNS was approved by the FDA for treatment of OAB in 2000. One drawback of PTNS is its invasive nature, requiring patients to present to a physician's office or clinic for treatment. Transcutaneous tibial nerve stimulation (TTNS) is a non-invasive alternative using electrodes placed on the skin. GEKO (Firstkind) was originally approved by the FDA in 2019 for prevention of deep vein thrombosis (DVT) after a stroke (Firstkind Ltd, 2019). It is now being studied for use in treating OAB and fecal incontinence in the home setting (Al-Danakh et al., 2022).
- ZIDA Wearable Neuromodulation System (ZIDA®—Exodus Innovations, Sufa, Israel) is an FDA-approved device indicated for the treatment of overactive bladder (OAB) and the associated symptoms of urinary urgency, urinary frequency, and urge incontinence. ZIDA Wearable Neuromodulation System utilizes sock-based, non-

invasive transcutaneous contacts that deliver a neuromodulation signal through the skin to the posterior tibial nerve.

- Cava & Orlin (2022) conducted a prospective, blinded, randomized, controlled trial including 40 individuals with Overactive Bladder (OAB) syndrome. The study included two groups: a treatment group which used an active ZIDA®activation device (ZIDA) utilizing Transcutaneous tibial nerve stimulation (TTNS) and a sham control group. Both groups self-administered the treatment once weekly for 30 minutes at home for a duration of 12 weeks. The ZIDA group reported an 80% success rate in treated symptoms of overactive bladder with a 71% reduction in episodes of incontinence and 62% reduction in episodes of urinary urgency. The authors noted several limitations of the study including a small sample size and problematic study design including a sham intervention.
- Schneider et al. (2015) conducted a systematic review of 16 studies including 469 individuals to evaluate the evidence on the safety and efficacy of TTNS for treating neurogenic lower urinary tract dysfunction (NLUTD). The authors noted that although preliminary data of RCTs and non-RCTs suggest TTNS might be effective and safe for treating NLUTD, the evidence base is poor, derived from small, mostly non-comparative studies with a high risk of bias and confounding. More reliable data from well-designed RCTs are needed to reach definitive conclusions.
- Ghavidel-Sardsahra et al. (2022) conducted a systematic review of nine studies including 11 trials to compare the safety and efficacy of Percutaneous and Transcutaneous posterior tibial nerve stimulation (PTNS and TTNS) and found that when PTNS or TTNS were compared to sham, placebo, no treatment, or conservative management, a decrease in frequency of urination was observed in both PTNS and TTNS. The authors concluded that nerve stimulations with either PTNS or TTNS appear to be effective interventions in treating refractory idiopathic OAB in terms of daily voiding frequency, maximum voided volume (MVV), urgency episodes, and nighttime voiding frequency. However, the results did not show any improvement in terms of urinary incontinence, post-void residual volume, urge incontinence, or maximum cystometric capacity.
- Patidar et al. (2015) conducted a single-blinded, prospective, sham controlled randomized trial including 40 children with non-neurogenic OAB refractory to behavioral and anticholinergic therapy. Participants were randomized to either a test group utilizing transcutaneous posterior tibial nerve stimulation or sham group.The OAB symptoms, severity of incontinence, number of voids daily (NV), average voided volume (AVV) and maximum voided volume (MVV) were evaluated before and after treatment. The AVV, MVV and NV improved significantly in test group as compared to the sham group. Moreover, 71.42% of individuals in the test group reported complete improvement in incontinence compared to only 12.5% of individuals in the sham group. The investigators concluded that TTNS is superior to placebo in treatment of non-neurogenic overactive bladder in children. However, the authors noted that the

study had a relatively short follow-up period of 12 weeks, and thus, relapse of OAB symptoms and maintenance schedule of TTNS need to be assessed further.
- Yang et al. (2021) conducted a meta-analysis of four trials (two randomized controlled trials, one retrospective study, and one before-after study) with 142 individuals to compare the safety and effectiveness of transcutaneous tibial nerve stimulation (TTNS) versus percutaneous tibial nerve stimulation (PTNS) in treating overactive bladder. Compared with PTNS, TTNS had a similar performance in the voiding frequency in 24 hours, the number of urgency episodes in 24 hours, the number of incontinence episodes in 24 hours, as well as in the nocturia frequency. No adverse events were identified in the TTNS group. The authors concluded that current data supported that TTNS is as effective as PTNS for the treatment of overactive bladder. However, the authors noted that the available evidence is low-grade and well-designed prospective studies with larger sample sizes are warranted.

**HCPCS E0738: Upper extremity rehabilitation system providing active assistance to facilitate muscle re-education, include microprocessor, all components and accessories**

Definitions/Background (HCPCS E0738)

An Upper extremity rehabilitation system providing active assistance to facilitate muscle re-education, include microprocessor, all components and accessories is a powered upper extremity rehabilitation system that consists of a biometric electroencephalogram (EEG) headset for use of the unaffected hemisphere, a powered upper extremity range of motion assist device, and a microprocessor control unit containing therapy software. The device detects electrical activity with electroencephalography and uses that information to drive an orthotic handpiece, thereby allowing the individual to engage in voluntary grasping movements.

Literature Review (HCPCS E0738)

- Brain-computer interface (BCI) technology is being studied for use in Parkinson's Disease, cluster headaches, tinnitus, and motor rehabilitation after stroke (Mridha et al., 2021).
- IpsiHand™ (Neurolutions, Santa Cruz, CA) is an FDA-approved device (FDA, April 2021) indicated for use in individuals with a history of chronic stroke (six months or more post-stroke) who are 18 years or older, undergoing stroke rehabilitation to facilitate muscle re-education and for maintaining or increasing range of motion in the upper extremities. The device is designed to use EEG signals from the non-lesioned hemisphere to control the handpiece (motorized glove) and complete the intended motion according to the type of signal detected. The IpsiHand™ System is contraindicated for individuals with severe spasticity or rigid contractures in the wrist and/or fingers, and for individuals with skull defects due to craniotomy or craniectomy.

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- A feasibility study (Bundy et al., 2017) examined whether a 12-week training period using an EEG-BCI system (IpsiHand™) led to functional improvements in ten chronic, hemiparetic stroke survivors. Motor function was evaluated before, during, and after the treatment. The subjects were assessed utilizing the Action Research Arm Test (ARAT) as the primary outcome measure. The mean scores resulted in a statistically significant average increase of 6.2 points in the Action Research Arm Test using the BCI-driven approach. However, the authors noted that larger randomized controlled trials are needed to determine the effectiveness of BCI-driven therapies.
- Humphries et al. (2022) conducted a non-randomized, prospective study to determine whether a contralesionally EEG-driven BCI reorganized brain networks for motor control. The study included eight individuals with upper limb hemiparesis at least six months post-stroke. Resting-state functional Magnetic Resonance Imaging (fMRI) scans and Median Upper Extremity Fugl-Meyer assessment (UEFM) data were recorded before and after the therapy period for 12 weeks. All BCI patients showed an increase in UEFM score after 12 weeks of contralesional BCI therapy. Clinically meaningful recovery occurred in seven of the eight patients. In addition, the authors noted that contralesional BCI therapy effectively enabled motor recovery for chronic hemiparesis. Moreover, motor functional connectivity strength and topographic extent decreased following BCI therapy. However, the authors noted that impact of this study was limited due to the small, non-randomized, prospective design. In addition, two study participants had multiple-stroke lesions, which may have further affected motor connectivity. The authors concluded that future studies with larger sample sizes are needed to explore the influence of BCI as a therapy for strokes affecting motor behavior.
- Rustamov et al. (2022) conducted a small, prospective study to investigate whether motor recovery using a contralaterally controlled BCI in individuals with chronic stroke was associated with alterations in phase-amplitude coupling (PAC) between gamma and lower frequency. Seventeen individuals with chronic stroke with upper limb hemiparesis completed BCI therapy for 12 weeks. Following 12 weeks of BCI therapy, all participants found an increase in the UEFM score. In addition to the motor functional improvement, the study found increased theta-gamma coupling in bihemispheric motor regions. The authors concluded that the findings support the notion that specific cross-frequency coupling dynamics in the brain likely play a mechanistic role in mediating motor recovery in the chronic phase of stroke recovery. However, the authors noted that the study has several limitations including a small sample size and lack of a BCI control group. The authors identified a need for additional carefully designed multicenter studies.

**HCPCS E0739: Rehab system with interactive interface providing active assistance in rehabilitation therapy, includes all components and accessories, motors, microprocessors, sensors**

Definitions/Background (HCPCS E0739)

A Rehab system with interactive interface providing active assistance in rehabilitation therapy, includes all components and accessories, motors, microprocessors, sensors describes a system comprised of a robotic exoskeleton and computer with an interactive interface to provide biofeedback on performance. The device is intended for use by individuals with a history of stroke and residual upper or lower extremity impairments to complete game-like training programs to challenge motor control. HCPCS E0739 was established to describe the Motus Hand and the Motus Foot.

Literature Review (HCPCS E0739)

- The Motus Hand and the Motus Foot (HCPCS E0739) are Class I devices exempt from the pre-market notification and approval procedures by the Food and Drug Administration (FDA).
- Mehrholz et al. (2018) conducted a Cochrane review including 45 randomized controlled trials with 1,619 participants to assess the effectiveness of electromechanical and robot-assisted arm training for improving activities of daily living, arm function, safety, and arm muscle strength in individuals after stroke. The authors concluded that electromechanical and robot-assisted arm training after stroke may improve activities of daily living scores, arm function, and arm muscle strength. However, the authors noted that the results must be interpreted with caution although the quality of the evidence was high, because there were variations between the trials in the intensity, duration, and amount of training; type of treatment; participant characteristics; and measurements used.
- A randomized controlled trial by Kutner, et al. (2010) including 17 individuals three to nine months post stroke examined the change in patient-reported, health-related quality of life associated with robotic-assisted therapy combined with reduced therapist-supervised training. Sixty hours of therapist-supervised repetitive task practice (RTP) was compared with a combined therapy group (30 hours of RTP combined with 30 hours of robotic-assisted therapy). Participants completed the Stroke Impact Scale (SIS) at baseline, immediately post-intervention, and two months post-intervention. Both groups had statistically significant improvement in activities of daily living scores, instrumental activities of daily living scores, and hand function from pre-intervention to post-intervention. The combined therapy group had a greater increase in rating of mood from pre-intervention to post-intervention, and the RTP-only group had a greater increase in rating of social participation from pre-intervention to follow-up. The combined therapy group had significant improvements in stroke recovery rating post-intervention and at follow-up, which appeared clinically significant; this also was true for stroke recovery rating from pre-intervention to follow-up in the RTP-only group. The authors concluded that robotic-assisted therapy may be an effective alternative or adjunct to therapist supervised task practice to enhance function recovery in individuals with a history of stroke. The authors cited a limitation of the study was the two groups received different numbers of RTP (the combined

therapy group received 30 hours of RTP compared with 60 hours for the RTP-only group).

- Linder et al. (2015) conducted a randomized trial to examined the effects of an eight-week home-based robot-assisted rehabilitation coupled with a home exercise program compared with a home exercise program alone on depression and quality of life (QOL) in 99 individuals less than six months after stroke. The primary QOL outcomes were the Stroke Impact Scale (SIS) and the Center for Epidemiologic Studies Depression Scale (CES–D). The results of the study demonstrated that both interventions were effective in improving QOL and depression outcomes. The authors noted that for individuals after stroke with limited access to traditional therapy, home-based interventions may be a valuable intervention for continued non-motor recovery. The authors noted several limitations of the study including the inability to rule out spontaneous recovery or compensatory strategies after stroke given the participants inclusion criteria of stroke within the previous six months. Moreover, the authors noted that the data was retrieved via self-report and thus future studies should include more objective measurement of compliance, such as a wrist accelerometer or similar technology, to better understand the dose-effect relationship.
- Wolf et al. (2015) conducted a randomized controlled trial to examine the efficacy of home-based telemonitored robotic-assisted therapy (Hand Mentor Pro) as part of a home exercise program (HEP) compared with a dose-matched HEP-only intervention among individuals less than six months post-stroke. The study included 99 hemiparetic participants with limited access to upper extremity rehabilitation. The participants were randomized to an experimental group which received combined HEP and HMP or a control group which received HEP only at an identical dosage. Both groups demonstrated improvement across all upper extremity outcomes including the Action Research Arm Test, Wolf Motor Function Test, and the Fugl Meyer Assessment (upper extremity). However, the authors noted multiple limitations to the study. The participants were less than six months post-stroke, and thus, spontaneous recovery may have contributed to functional motor improvement. Moreover, the authors reported multiple problems with the study design. The authors concluded that although the telerehabiliation component may be valuable in individuals post-stroke with limited resources, future studies are needed to determine the efficacy of this intervention.

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