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Percutaneous Electrical Nerve Field Stimulation for Irritable Bowel Syndrome

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Coverage

Percutaneous electrical nerve field stimulation for abdominal pain in individuals with irritable bowel syndrome is considered **is considered experimental, investigational and/or unproven.**

Policy Guidelines

None.

Description

Percutaneous electrical nerve field stimulation involves the transmission of electrical impulses to cranial nerve bundles in the ear targeting brain areas involved in processing pain. In the case of patients with irritable bowel syndrome, nerves processing pain for the abdominal region are targeted.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is estimated to affect 5% to 10% of the population globally, and accounts for between 2.4 and 3.5 million physician visits in the United States each year. (1) Up to two-thirds of patients with IBS are female, and it is most common in patients less than 50 years of age. The cause of IBS remains unknown, but is believed to be due to a dysfunction in gut-brain interaction. (2) Symptoms of IBS can include diarrhea, constipation, or both. Abdominal pain and bloating are also common IBS symptoms. These symptoms decrease patient quality of life and create a significant healthcare burden. (3) The American College of Gastroenterology (ACG) recommends that patients diagnosed with IBS are categorized by subtypes: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with mixed symptoms (IBS-M), or IBS without abnormal stools (IBS-U).

Treatment

First-line treatment of patients with IBS generally involves dietary changes. If dietary changes fail to achieve therapeutic goals, there are numerous pharmacotherapeutic options for patients with IBS. Pharmacologic treatment is based on the IBS subtype, and the predominance of either constipation or diarrhea (Table 1). (3-5) Notably, many IBS treatments are not Food and Drug Administration (FDA)-approved for children or adolescents. The American College of Gastroenterology recommends that gut-directed psychotherapy such as cognitive-behavior therapy and gut-directed hypnotherapy may be beneficial for global IBS symptoms. (3)

Table 1. Pharmacologic Treatment of Irritable Bowel Syndrome

IBS-D	IBS-C	Abdominal Pain
Antidiarrheal agents (e.g., loperamide)	Laxatives (e.g., polyethylene glycol)	Antispasmodics (e.g., dicyclomine, hyoscyamine, peppermint oil)
Mu-opioid receptor agonist (eluxadoline for refractory patients only)	Chloride channel activator (lubiprostone)	TCA
5-HT3 receptor antagonist (alosetron or ondansetron)	Guanylate cyclase agonists (linaclotide or plecanatide)	SSRI
Antibiotic (rifaximin)	Sodium/hydrogen exchanger 3 (tenapanor)	

HT: hydroxytryptamine (serotonin); IBS-C: irritable bowel syndrome with constipation; IBS-D: irritable bowel syndrome with diarrhea; SSRI: selective serotonin reuptake inhibitor; TCA: tricyclic antidepressant.

Percutaneous Electrical Nerve Field Stimulation

Because there are few pharmacologic treatments for children and adolescents with IBS, nonpharmacologic options are commonly explored. Percutaneous electrical nerve field stimulation (PENFS) is a potential treatment option for these patients. PENFS involves a non-implantable device which stimulates nerves remotely from the site of pain and has been studied for a variety of musculoskeletal or neuropathic pain conditions or for patients with

opioid withdrawal. (6) The IB-Stim device is a type of PENFS that is intended for use only in patients with IBS. The device is disposable and battery-operated. Key components of the device include a percutaneous electrical nerve field stimulator placed behind the ear which connects to a multi-wire electrode array consisting of 4 leads. The electrodes have thin needles and attach to the ear at points (preauricular, lobule and superior crus) where cranial nerve peripheral branches are located just beneath the skin. A pen light included with the device is used to visualize the neurovasculature features and aid in proper electrode placement.

Regulatory Status

In 2019, the IB-Stim device (previously known as Neuro-Stim; Innovative Health Solutions, Inc.) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the de novo 513(f)(2) process (DEN180057). Both the IB-Stim and the similar NSS-2 BRIDGE device (Innovative Health Solutions, Inc.) are derivatives of the Electro Auricular Device (Navigant Consulting, Inc.). The IB-Stim device is indicated for patients 11 to 18 years of age with functional abdominal pain associated with IBS when combined with other IBS therapies. It is intended to be used for 120 hours per week up to 3 consecutive weeks. The First Relief v1 (DyAnsys, Inc.) device was deemed substantially equivalent to the IB-Stim device in 2020. FDA product code: QHH.

Rationale

This medical policy was created with a search of the PubMed database. The most recent literature update was performed through June 12, 2024.

Medical policies assess the clinical evidence to determine whether the use of a 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 patients and to 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 a technology, 2 domains are examined: the relevance and the 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. Randomized controlled trials 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.

Irritable Bowel Syndrome

Clinical Context and Therapy Purpose

The purpose of percutaneous electrical nerve field stimulation (PENFS) in individuals who have irritable bowel syndrome (IBS) 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 policy.

Populations

The relevant population of interest is individuals with abdominal pain related to IBS.

Interventions

The therapy being considered is PENFS with the IB-Stim device.

Comparators

The following therapies are currently being used to treat IBS: dietary modification, behavior modification, and pharmacotherapy.

Outcomes

The general outcomes of interest are pain, bowel function, and quality of life. Follow-up at 3 months is of interest to monitor outcomes.

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.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Controlled Trials

Kovacic et al. (2017) conducted an RCT comparing the Neuro-Stim PENFS device with a sham device in adolescent patients with abdominal pain-related functional gastrointestinal disorders including IBS (Table 2). (7) Patients 11 to 18 years of age with abdominal pain (pain score ≥3 on an 11-point scale) occurring at least twice weekly for at least 2 months were included. The devices were worn for 5 days each week for 4 weeks. Baseline medications were continued

with the exception of antispasmodics which were not allowed during the study period. Enrolled patients were primarily female (91%) and White (90%). Pain, as measured on the Pain Frequency-Severity-Duration (PFSD), was the primary outcome. The PFSD scale incorporates several aspects of the pain experience and is generally calculated over a 14-day period but was modified as a weekly score in this trial with a high composite score of 70. Both "worst pain" and median PFSD composite scores were better with PENFS than placebo (Table 3). The Symptom Response Scale (-7 to +7 [with negative scores as worse and positive scores as better]) was used to assess the overall symptoms. Although the authors reported statistically significantly improved scores with the Neuro-Stim device at 3 weeks (Table 3), numerical differences between groups were small. Longer-term pain scores obtained at a median of 9.2 weeks after treatment remained improved from baseline in the active treatment group with a decrease of composite PFSD scores of -8.4 compared with 0.0 in the sham group. Adverse events including ear discomfort and adhesive allergy were similar between groups. The study is limited by the small sample size, the heterogeneous population of gastrointestinal disorders, lack of bowel habit measurement, and short duration of follow-up. Krasaelap et al. (2020) evaluated a subgroup of 50 patients with IBS from the Kovacic et al. (2017) RCT (Table 2). (8) At 3 weeks there were more responders with the active treatment (response defined as ≥30% reduction in worst abdominal pain) than with the sham device (Table 3). At the extended follow-up (8-12 weeks), the percentage of responders was similar between groups (32% vs. 18%; p=.33).

Table 2. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Kovacic et al. (2017) (7)	US	1	2015-2016	Adolescents (11-18 years of age) with abdominal pain related to a functional GI disorder	Neuro-Stim (n=60)	Sham (n=55)
Krasaelap et al. (2020) (8)[a]	US	1	2015-2016	Adolescents (11-18 years of age) with abdominal pain related to IBS	Neuro-Stim (n=27)	Sham (n=23)

GI: gastrointestinal; IBS, irritable bowel syndrome; RCT: randomized controlled trial.
[a]A subgroup analysis of Kovacic et al. (2017).

Table 3. Summary of Key RCT Results

Study	Worst Pain (Week 3)	PFSD Composite Score (Week 3)	Worst Pain Decrease of ≥30% from Baseline to Week 3	Average Pain Decrease of ≥30% from Baseline to Week 3	SRS (Week 3)
Kovacic et al. (2017) (7)	N=104	N=104	N=93	N=93	N=104

PENFS	Median 5.0 (IQR, 4.0-7.0)	Median 8.4 (IQR, 3.2-16.2)	29 (60%)	28 (58%)	Median 3.0 (IQR, 1.0-4.8)
Sham	Median 7.0 (IQR, 5.0-9.0)	Median 15.2 (IQR, 4.4-36.8)	10 (22%)	13 (29%)	Median 1.0 (IQR, 0.0-2.3)
LSM (95% CI); p-value	2.15 (1.37-2.93); <.0001	11.48 (6.63-16.32); <.0001	NR; .00031	NR; p=.007	NR; .0003
Krasaelap et al. (2020) (8)	N=50	N=50	N=50		N=50
PENFS	Median 5.0 (IQR, 4.0-7.0)	Median 7.5 (IQR, 3.6-14.4)	16 (59%)		Median 3.0 (IQR, 2-4)
Sham	*Median 7.0 (IQR, 5.0-9.0)*	*Median 14.4 (IQR, 4.5-39.2)*	*6 (26%)*		*Median 0 (IQR, 0-2)*
LSM (95% CI); p-value	NR; .0074	NR; .026	NR; .024		NR; .003
NNT			3		

CI: confidence interval; IQR, interquartile range; LSM: least squares mean; NNT: number needed to treat; NR: not reported; PENFS: percutaneous electrical nerve field stimulation; PFSD: Pain Frequency-Severity-Duration; RCT: randomized controlled trial; SRS: symptom response scale.

The purpose of the study limitations tables (see Tables 4 and 5) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement. Limitations are only reported from the Kovacic et al. (2017) study as those in the subgroup analysis by Krasaelap et al. (2020) mirror the parent study.

Table 4. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Kovacic et al. (2017) (7)	4. Largely White, female population			1. No bowel habit outcomes included; 4. Use of modified PFSD for pain outcomes	1,2. Median follow-up duration of 9.2 weeks

PFSD: Pain Frequency-Severity-Duration.
The study limitations stated in this table are those notable in the current literature review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not established and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 5. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Kovacic et al. (2017) (7)				6. Modified intention-to-treat analysis excluding patients with <1 week of data or diagnosis of organic disease after enrollment		

The study limitations stated in this table are those notable in the current literature review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Section Summary: Irritable Bowel Syndrome

One RCT was identified evaluating the use of PENFS for patients with abdominal pain-related functional gastrointestinal disorders including IBS. Despite finding improved pain and symptoms at the end of the treatment period (3 weeks) with the active device compared with sham, the

differences between groups by 12 weeks were minimal. A subgroup analysis limited to patients with IBS (N=50) had similar results. The study is limited by its small sample size, heterogeneous population of gastrointestinal disorders, lack of bowel habit measurement, and the short duration of follow-up.

UpToDate

An UpToDate article on management of functional abdominal pain (FAP) in children and adolescents characterized the use of PENFS for relief of FAP in adolescents with IBS as "promising" but stated that additional confirmatory studies are needed to confirm results, determine the optimal setting and duration of treatment, and determine the optimal target population, before it can be routinely recommended. (9)

Summary of Evidence

For individuals with irritable bowel syndrome (IBS) who receive percutaneous electrical nerve field stimulation (PENFS), the evidence includes a subgroup analysis of a single randomized controlled trial (RCT). Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCT (N=115) included a heterogeneous population of adolescent patients aged 11 to 18 years with pain-related functional gastrointestinal disorders. Treatment was administered for 3 weeks, and reductions in pain were observed with the active device compared with a sham PENFS device at end of treatment and end of follow-up (maximum of 12 weeks). The subgroup of patients with IBS also had improved pain at the end of treatment with the active device compared with the sham device. However, the trial is limited by its small sample size, heterogeneous population of gastrointestinal disorders, lack of bowel habit measurement, and the short duration of follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American College of Gastroenterology

The American College of Gastroenterology (ACG) updated their recommendations for irritable bowel syndrome (IBS) management in 2021. (3) The ACG recommendations do not include PENFS.

The American Gastroenterological Association

The American Gastroenterological Association (AGA) updated guidelines for both IBS with constipation and IBS with diarrhea in 2022. (4, 5) Neither of these guidelines include recommendations for PENFS.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 6.

Table 6. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date

Ongoing			
NCT04428619	Neuromodulation With Percutaneous Electrical Nerve Field Stimulation for Adults With Irritable Bowel Syndrome: A Randomized, Double-Blind, Sham-Controlled Pilot Study	54	Nov 2024

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	0720T
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
11/01/2024	New medical document. Percutaneous electrical nerve field stimulation for abdominal pain in individuals with irritable bowel syndrome is considered is considered experimental, investigational and/or unproven.