Policy Number	**PSY301.025**
Policy Effective Date	**12/15/2025**

Digital Health Technologies: Therapeutic Applications

Table of Contents

Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

The use of Freespira **is considered experimental, investigational and/or unproven** for all indications including treatment of panic disorder and/or post-traumatic stress disorder (PTSD).

The use of NightWare **is considered experimental, investigational and/or unproven** for all indications including treatment of nightmare disorder or nightmares from PTSD.

Policy Guidelines

None.

Description

Digital health technologies is a broad term that includes categories such as mobile health, health information technology, wearable devices, telehealth and telemedicine, and personalized medicine. These technologies span a wide range of uses, from applications in

general wellness to applications as a medical device, and include technologies intended for use as a medical product, in a medical product, as companion diagnostics, or as an adjunct to other medical products (devices, drugs, and biologics). The scope of this review includes only those digital technologies that are intended to be used for therapeutic application and meet the following 3 criteria: 1) Must meet the definition of "Software as a medical device" which states that software is intended to be used for a medical purpose, without being part of a hardware medical device or software that stores or transmits medical information. 2) Must have received marketing clearance or approval by the U.S. Food and Drug Administration (FDA) either through the *de novo* premarket process or 510(k) process or pre-market approval and 3) Must be prescribed by a healthcare provider.

Scope of Policy

Software has become an important part of product development and is integrated widely into digital platforms that serve both medical and non-medical purposes. The 3 broad categories of software use in medical devices are:

1. Software used in the manufacture or maintenance of a medical device (e.g., software that monitors x-ray tube performance to anticipate the need for replacement);
2. Software that is integral to a medical device or software in a medical device (e.g., software used to "drive or control" the motors and the pumping of medication in an infusion pump);
3. Software, which on its own is a medical device referred to as "Software as a Medical Device" (SaMD) (e.g., software that can track the size of a mole over time and determine the risk of melanoma).

The International Medical Device Regulators Forum, a consortium of medical device regulators from around the world led by the U.S. Food and Drug Administration (FDA) defines SaMD as "software that is intended to be used for one or more medical purposes that perform those purposes without being part of a hardware medical device". (1) Such software was previously referred to by industry, international regulators, and health care providers as "standalone software," "medical device software," and/or "health software," and can sometimes be confused with other types of software.

The scope of this policy includes only those digital technologies that are intended to be used for therapeutic application and meet the following 3 criteria:

1. Must meet the definition of "Software as a medical device" (SaMD) which states that software is intended to be used for a medical purpose, without being part of a hardware medical device or software that stores or transmits medical information.
2. Must have received marketing clearance or approval by the U.S. FDA either through the *de novo* premarket process or 510(k) process or pre-market approval and,
3. Must be prescribed by a healthcare provider.

Evaluation Framework for Digital Health Technologies

SaMDs, as defined by the FDA, are subject to the same evaluation standards as other devices; technology evaluation criterion are as follows:

1. The technology must have final approval from the appropriate governmental regulatory bodies.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.
3. The technology must improve the net health outcome.[a]
4. The technology must be as beneficial as any established alternatives.
5. The improvement must be attainable outside the investigational settings.[b]

[a] The technology must assure protection of sensitive patient health information as per the requirements of The Health Insurance Portability and Accountability Act of 1996 (HIPAA).
[b] The technology must demonstrate usability in a real-world setting.

Other regulatory authorities such as the United Kingdom's National Institute for Health and Care Excellence (NICE) have proposed standards to evaluate SaMD. (2)

Regulatory Status
Digital health technologies that meet the current scope of the policy are shown in Table 1.

Table 1. Examples of Prescription Digital Health Applications

Freespira® (Canary Breathing System)	
Manufacturer	Freespira (previously PaloAlto Health Sciences)
FDA Cleared Indication	Freespira is intended for use as a relaxation treatment for the reduction of stress by leading the user through guided and monitored breathing exercises. The device is indicated as an adjunctive treatment of symptoms associated with panic disorder and/or PTSD, to be used under the direction of a healthcare professional, together with other pharmacological and/or non-pharmacological interventions.
Description	It is a small breathing sensor with a tablet that is used twice a day for 17 minutes. Individuals are trained to use the Sensor with the Mobile App to measure and display their $EtCO_2$ level and RR and how different breathing habits affect $EtCO_2$ levels.
FDA Product Codes	HCC, CCK
Clearance	K131586, K180173
Date	2013 2018
NightWare™	
Manufacturer	NightWare, Inc.
FDA Cleared Indication	The NightWare digital therapeutic is indicated to provide vibrotactile feedback on an Apple Watch based on an analysis of heart rate and motion during sleep for the temporary reduction of sleep disturbance related to nightmares in adults 22 years or older who suffer from nightmare disorder or have nightmares from PTSD. It is intended for home use.

Description	The NightWare is a therapeutic platform using a proprietary Apple Watch® application. The app learns the wearer's sleep patterns and customizes treatment to the individual. The app monitors the wearer's heart rate and movement while sleeping and arouses the wearer with a vibration alert when a stress threshold is reached so as not to awaken the individual. Users wear the watch only while sleeping and not during the day.
FDA Product Codes	QMZ
Clearance	Breakthrough device designation
Date	2020

$EtCO_2$: exhaled carbon dioxide; FDA: U.S. Food and Drug Administration; PTSD: post-traumatic stress disorder; RR: respiration rate.

Rationale

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 individuals 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 one 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.

Panic Disorder and Post-Traumatic Stress Disorder

Clinical Context and Therapy Purpose

Panic disorder is an anxiety disorder associated with marked impairment in social and occupational functioning, significant impact on quality of life, and high utilization of health care services. (3) Fearful interpretation of bodily symptoms such as tachycardia, shortness of breath, chest tightness, and dizziness with catastrophic beliefs is the core of the diagnosis and differentiates it from other anxiety disorders. Many individuals with panic disorder

hyperventilate and it has been suggested that respiratory abnormality associated with panic disorder may be due to a hypersensitivity to carbon dioxide (CO_2). Based on the recognition of subtle respiratory irregularities associated with hyperventilation in individuals with panic disorder, and CO_2 sensitivity, Meuret et al. (2008) developed a breathing intervention focused on normalizing both exhaled carbon dioxide levels (EtCO2) and respiratory rate. (4) The protocol provided breath-to-breath feedback of EtCO2, while modeling paced breathing at 4 different respiratory rates. Administered as twice daily, 17-min sessions over a 4-week period, the authors reported that by study end, 86% of subjects reported zero weekly panic attacks; an improvement that was durable over time, as 73% reported zero weekly attacks 1-year post-treatment. Freespira incorporates this protocol in their approach to managing panic disorder.

Post-traumatic stress disorder (PTSD) is marked by symptoms of hyperarousal, difficulties with emotional regulation, negative affect, and autonomic dysfunction. (5) Carbon dioxide hypersensitivity may be responsible for mediating some PTSD symptoms as CO_2 challenge tests in individuals with established PTSD have been shown to provoke a panic attack. (6, 7) Since the characteristic of CO_2 hypersensitivity is shared by both PTSD and panic disorder, extending the use of Freespira to a population with PTSD is a logical and potentially valuable clinical tool given the lack of medication-free treatment options for PTSD.

The purpose of prescribed therapeutic digital applications is to provide a treatment option that is an alternative to or an improvement on existing therapies for individuals with panic disorder and PTSD. Panic symptoms may be associated with more shallow and rapid breathing. Freespira addresses rapid and shallow breathing that may contribute to panic symptoms through training of respiratory control.

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

Populations
The relevant populations of interest are individuals with panic disorder and PTSD.

Interventions
The digital therapy being considered is Freespira.

Freespira consists of biofeedback software that monitors respiratory rate and CO_2 and provides feedback to the user via a tablet on expiration and respiratory rate in order to control breathing. The treatment includes a proprietary handheld CO_2 sensor, nasal cannula, and tablet with pre-loaded software. The user is instructed to complete two 17-minute sessions per day for 4 weeks, with weekly check-in with a therapist. Target respiratory rate is 13 during week 1, 11 during week 2, 9 during week 3, and 6 during week 4.

Comparators
The following practice is currently being used to treat mental health disorders: medications and in-person psychological and behavioral therapy.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Follow-up after treatment and at 6 to 12 months following the end of treatment is of interest to monitor outcomes.

Outcome measures for panic disorder and PTSD are described in Table 2.

Table 2. Outcome Measures

Outcome	Measure (Units)	Description and Administration	Thresholds for Improvement/Decline or Clinically Meaningful Difference
CAPS-5	Clinician Administered PTSD Scale	30-item clinician-administered scale that rates the severity of PTSD symptoms drawn from DSM-5 criteria (see Appendix).	Response is a 13-point change. Remission is a CAPS-5 score <5.
CGI-S	Clinical Global Impression Severity	A single-item clinician-rated measure of severity of psychopathology, using a 7-point Likert scale ranging from 'normal' to 'among the most extremely ill individuals.'	
CHRT-SR	Concise Health Risk Tracking Self-Report	12-item self-report inventory that assesses suicidal and related thoughts.	
C-SSRS	Columbia Suicide Severity Rating Scale	Measures suicidal ideation.	
$EtCO_2$	End-tidal carbon dioxide, mm Hg	CO_2 monitor.	Normal is >35 mm Hg.
PHQ-9	The Patient Health Questionnaire 9-item depression scale	Self-report scale that asks individuals to rate the presence of DSM-4 symptom criteria ranging from '0' (not at all) to '3' (nearly every day).	

PDSS	Panic Disorder Severity Scale	7-item clinician-rated scale that indicates the severity and frequency of panic symptoms, fear of subsequent attacks, and avoidance behaviors.	Response is a 40% or greater reduction in scores. A score of 5 or less is considered remission.
SF-36	36-item Short Form Health Survey	Self-rated survey of health impact on daily function.	

PTSD: post-traumatic stress disorder; DSM: Diagnostic and Statistical Manual of Mental Disorders; CO_2: carbon dioxide; mm Hg: millimeters of mercury.

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.

Two pivotal single-arm studies have been reported on the Freespira app for panic disorder (8) and PTSD. (9) Study characteristics and results of these studies are summarized in Tables 3 and 4, respectively. No limitations in study relevance were noted. Multiple limitations in design and conduct summarized in Table 5 preclude the meaningful interpretation of their findings. Both studies have significant dropout rate and consequently data is missing for more than 30% of study participants in both studies. For example, study dropout rate was 33%, 39%, and 52% at 2, 6, and 12 months of follow-up in Tolin et al. (2017) and 24% and 31% at 2 and 6 months of follow-up in Ostacher et al. (2021). No clear description of reasons for missingness, characteristics of missing observations, or sensitivity analyses of missing data assumptions were provided. In addition to the 2 pivotal studies, 1 single-arm study published by Kaplan et al. (2020) funded by a payer (Highmark Health) reported findings in 52 individuals with a diagnosis of panic disorder. (10) The primary goal of this study was to determine if treatment with Freespira in individuals with panic disorder would significantly reduce the cost of care in the 12 months following treatment. This single-arm study suffers from similar drawbacks as the first 2 pivotal studies.

Table 3. Summary of Key Study Characteristics for Freespira

Tolin et al. (2017) (8)	
Study Design	Single-arm trial

Setting	Multi-site (4 sites, 2016)
Participants	Inclusion: • Adults aged 18 to 65 years with a primary diagnosis of panic disorder using Mini International Diagnostic Interview • Rated as "moderately ill" or greater on the CGI-S • Either off medications or stable on medications for at least 3 months Exclusion: • Receiving other psychological treatment • Unresponsive to cognitive-behavioral therapy • Evidence of organic mental disorder, severe suicidality, psychotic disorder, substance dependence, uncontrolled cardiovascular or pulmonary disease, or seizures
Interventions	Twice a day 17-minute home sessions with Freespira for 4 weeks (N=69)
Ostacher et al. (2021) (9)	
Study Design	Single arm trial
Setting	Single center (2017 to 2019)
Participants	Inclusion: • Adults 18 years and older with a primary DSM-5 diagnosis of PTSD (see Appendix) • CAPS-5 score of ≥30, CGI-S score of ≥4 • Stable psychotropic medication Exclusion: • Any concurrent evidenced-based therapy for PTSD • Concurrent psychotic disorder, alcohol or drug use disorder requiring acute medical treatment, epilepsy or recent seizures; and cardiovascular or pulmonary disease
Interventions	Twice a day 17-minute home sessions with Freespira for 4 weeks (N=55)
Kaplan et al. (2020) (10)	
Study Design	Single arm trial
Setting	Single health system (multiple sites)
Participants	Inclusion: • Adults 18 and older with primary diagnosis of panic disorder • CGI-S ≥4 (moderately ill) • Either off medications or stable on medications prior to, during, or immediately after the 4-week Freespira treatment Exclusion: • Receiving other psychological treatment • Evidence of organic mental disorder, severe suicidality, psychotic disorder, substance dependence, uncontrolled cardiovascular or pulmonary disease, or seizures

Interventions	Twice a day, 17-minute home sessions with Freespira for 4 weeks, with weekly check-in visits to their therapist (N=52)

CAPS-5: Clinician Administered PTSD Scale; CGI-S: Clinical Global Impression Severity; DSM: Diagnostic and Statistical Manual of Mental Disorders; PTSD: Post-traumatic stress disorder.

Table 4. Summary of Key Study Results for Freespira

Tolin et al. (2017) (8)	
PDSS (±SD)	Baseline: 14.8 (±3.6) Post-treatment: 5.4 (±4.4) Change versus baseline: 9.4 At 2-month follow-up: 6.0 (±5.2) Change versus baseline: 8.8 At 12-month follow-up: 5.0 (±6.2) Change versus baseline: 9.4
Responder/Remission at 12 months	Response[a]: 81.8% Remission[b]: 69.7%
Participant Flow	Enrolled: 69 Received treatment: 66 (96%) Completed treatment: 53 (77%) Completed post-treatment assessment: 48 (70%) Completed 2-month follow-up: 46 (67%) Completed 6-month follow-up: 42 (61%) Completed 12-month follow-up: 33 (48%)
Ostacher et al. (2021) (9)	
CAPS-5 Score (± SD)	Baseline: 49.5 (±9.2) Post-treatment: 31.8 (±14.1) Change versus baseline: 17.7 At 2-month follow-up: 27.1 (±17.8) Change versus baseline: 22.4 At 6-month follow-up: 26.2 (±18.4) Change versus baseline: 23.4
Responder/Remission at 2 months	Response[c]: 88% (95% CI 74% to 96%) Remission[d]: 48%
Participant Flow	Enrolled: 55 Received treatment: 55 (100%) Completed treatment: 48 (87%) Completed Post treatment assessment: 48 (87%) Completed 2-month follow-up: 42 (76%) Completed 6 months follow-up: 38 (69%)
Kaplan et al. (2020) (10)	
PDSS (± SD)	Baseline: 14.4 (±3.8) Post-treatment: 4.9 (±3.4) Change versus baseline: 9.5

	At 6-month follow-up: 4.1 (±4.3) Change versus baseline: 10.3 At 12-month follow-up: 4.4 (±4.5) Change versus baseline: 10
Responder/Remission at 12 months	Response[a]: 91% Remission[b]: 68%
Participant Flow	Enrolled: 52 Received treatment: 50 (96%) Completed Post treatment assessment: 44 (85%) Completed 2-month follow-up: 27 (52%) Completed 6 months follow-up: 22 (42%)

CAPS-5: Clinician Administered PTSD Scale; PDSS: panic disorder severity scale; PTSD: post-traumatic stress disorder; SD: standard deviation.

[a] 40% or greater reduction in scores on the PDSS.

[b] Score of 5 or less on the PDSS.

[c] Percent of individuals having ≥ 6-point decrease in CAPS-5 at 2 months.

[d] Percent of individuals who meet the criteria for response plus no longer meeting DSM-5 criteria for PTSD and having a CAPS-5 score < 25.

Table 5. Study Design and Conduct Limitations for Freespira

Study	
Tolin et al. (2017) (8)	
Allocation[a]	1. Participants not randomly allocated; 4. Inadequate control for selection bias;
Blinding[b]	1.Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician;
Selective Reporting[c]	
Data Completeness[d]	1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 6. Not intent to treat analysis (ITT analysis reported but definition of ITT is unclear);
Power[e]	1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference;
Statistical[f]	3. Confidence intervals and/or p values not reported; 5. Other (missing/unclear information on following: definition of intention to treat, primary hypothesis, primary outcome and its timing, reason for missing data, lack of control for type I error for multiple statistical comparisons and whether definitions of response and remission were pre-specified).
Ostacher et al. (2021) (9)	
Allocation[a]	1. Participants not randomly allocated;

	4. Inadequate control for selection bias;
Blinding[b]	1.Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician;
Selective Reporting[c]	
Data Completeness[d]	1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 6. Not intent to treat analysis (ITT analysis reported but definition of ITT is unclear);
Power[e]	1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference;
Statistical[f]	3. Confidence intervals and/or p values not reported; 5. Other (missing/unclear information on following: definition of intention to treat, primary hypothesis, primary outcome and its timing, reason for missing data, lack of control for type I error for multiple statistical comparisons and whether definitions of response and remission were pre-specified)
Kaplan et al. (2020) (10)	
Allocation[a]	1. Participants not randomly allocated; 4. Inadequate control for selection bias;
Blinding[b]	1.Participantsor study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician;
Selective Reporting[c]	1. Not registered
Data Completeness[d]	1. High loss to follow-up or missing data; 2. Inadequate handling of missing data;
Power[e]	
Statistical[f]	3. Confidence intervals and/or p values not reported;

ITT: intention to treat.

The study limitations stated in this table are those notable in the current 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: Panic Disorder and Post-Traumatic Stress Disorder

Panic symptoms in panic disorder and PTSD have been associated with more shallow and rapid breathing. The prescription digital therapy Freespira provides feedback to the user to learn to slow the breathing rate over a training period of 4 weeks. The evidence on Freespira for individuals with panic disorder includes 2 single-arm studies and 1 single-arm study in individuals with PTSD. All of the studies report an improvement in symptoms, but are limited by loss to follow-up ranging from 24% to 58% and multiple limitations in the design and conduct. A well-designed blinded RCT with a clear design for testing a pre-specified hypothesis is needed. Given the high loss to follow-up and lack of a control group in these studies, the benefit of a 4-week program of respiratory biofeedback in individuals with panic disorder and PTSD is uncertain.

Nightmare Disorder and Post-Traumatic Stress Disorder-Associated Nightmares

Clinical Context and Therapy Purpose

The purpose of prescribed therapeutic digital applications is to provide a treatment option that is an alternative to or an improvement on existing therapies for individuals with nightmare disorder and PTSD-associated nightmares.

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

Populations

The relevant populations of interest are individuals with nightmare disorder and PTSD-associated nightmares.

Interventions

The digital therapy being considered is NightWare. The device is intended to reduce nightmares in individuals with nightmare disorder and PTSD-associated nightmares in conjunction with standard therapy.

NightWare uses an artificial intelligence algorithm to learn an individual's normal and abnormal sleeping heart rate and motion in conjunction with an Apple Watch, Apple iPhone, and NightWare server. Upon detection of abnormal activity, the watch provides short vibrations to disrupt the nightmare without waking the patient. The watch is intended to be worn only during sleep and is used in addition to usual treatment for PTSD-associated nightmares and nightmare disorder.

Comparators

The following practices are currently being used to treat PTSD-associated nightmares: medications; image rehearsal therapy; cognitive behavioral therapy (CBT); cognitive behavioral therapy for insomnia (CBT-I); eye movement desensitization and reprocessing; exposure, relaxation, and rescripting therapy. (11)

The following practices are currently being used to treat nightmare disorder: medications; image rehearsal therapy; CBT; exposure, relaxation, and rescripting therapy; hypnosis; lucid dreaming therapy; progressive deep muscle relaxation; sleep dynamic therapy; self-exposure therapy; systematic desensitization; testimony method. (11)

Outcomes

The general outcomes of interest are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Follow-up after treatment and at 6 to 12 months following the end of treatment is of interest to monitor outcomes.

Outcome measures for nightmare disorder and PTSD-associated nightmares are described in Table 6.

Table 6. Outcome Measures

Outcome	Measure (Units)	Description and Administration	Thresholds for Improvement/Decline or Clinically Meaningful Difference (if known)
ESS	Epworth Sleepiness Scale	The ESS is a short, self-administered questionnaire that asks individuals how likely they are to fall asleep in 8 different situations (e.g., watching TV, sitting quietly in a car, or sitting and talking to someone).	The scale ranges from 0 to 24. An ESS of ≥10 is considered excessively sleepy. A decrease of 2 points is considered the clinically meaningful difference.
PHQ-0	The Patient Health Questionnaire 9-item depression scale	Self-report scale that asks individuals to rate the presence of DSM-4 symptom criteria ranging from '0' (not at all) to '3' (nearly every day).	
PSQI	Pittsburgh Sleep Quality Index	17-item self-rated questionnaire on initiating and maintaining sleep, and	Clinically meaningful difference is 3 points.

		on sleep-related daytime function.	
PSQI-A	Pittsburgh Sleep Quality Index-Addendum	Assesses PTSD-related sleep quality.	
SF-36	36-item Short Form Health Survey	Self-rated survey of health impact on daily function.	

DSM: Diagnostic and Statistical Manual of Mental Disorders; PTSD: post-traumatic stress disorder.

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.

One pivotal double-blind sham-controlled RCT (NCT04040387) conducted in a Veterans Administration Center has been reported in the manufacturers "Instructions for Use". (12, 13)

Study characteristics and results of this trial are summarized in Tables 7 and 8 respectively. The trial was designed to enroll 240 participants with PTSD and nightmares, however, only 70 were enrolled. Data from 63 trial participants were included on the primary and secondary outcome measures. The primary outcome was the difference in the Pittsburg Sleep Quality Index (PSQI). The change from baseline was numerically higher for the NightWare group compared to sham, but the difference did not achieve statistical significance. There was no statistical difference observed in multiple other secondary endpoints such as change from baseline to day 30 in the active treated arm versus sham in the following outcome measures: PTSD Checklist for DSM-5 (PCL-5), Patient Health Questionnaire 9-item depression scale (PHQ-9), Trauma-Related *Nightmare* Survey (TRNS), Functional Outcomes of Sleep Questionnaire (FOSQ-10), and Veterans RAND 12 Item Health Survey (VR-12). The 2 primary safety measures of Nightmare device were to assess worsening of daytime sleepiness as assessed by the Epworth Sleepiness Scale (ESS) and increase in suicidality as assessed by the Columbia Suicide Severity Rating Scale (CSSRS).

Multiple limitations in design and conduct are summarized in Table 9 and preclude meaningful interpretation of study findings. This trial failed to achieve recruitment goals and was likely underpowered.

Table 7. Summary of Key RCT Characteristics for NightWare

FDA De Novo Summary for NightWare (NCT04040387) (12)	
Study Design	Double-blind RCT
Setting	Single-center (2019 to 2020)
Participants	Inclusion: • Documented diagnosis of PTSD (DSM 4 or 5 diagnostic criteria) (see Appendix) • 22 years of age or older • PSQI score 10 or more at screening • Have repetitive nightmares contributing to disrupted sleep as reported by the participant Exclusion: • High suicide risk including current suicidal ideation • Cardiovascular comorbidities (uncontrolled atrial fibrillation) • Use of varenicline, beta-blockers, non-dihydropyridines • Circadian rhythm disruption on a regular basis (shiftwork) • Other sleep- and nightmare-related comorbidities • Active substance use Primary Outcome: • Change in average PSQI score from day 0 to day 30 between active versus sham arm
Interventions	
Active	Individuals wore an Apple Watch with artificial intelligence software that produced short vibrations when sleep disturbance was detected.
Control	Sham system consisting of an Apple watch with software but the watch did not vibrate during the night.

DSM: Diagnostic and Statistical Manual of Mental Disorders; FDA: Food and Drug Administration; PSQI: Pittsburgh Sleep Quality Index; PTSD: post-traumatic stress disorder; RCT: randomized controlled trial.

Table 8. Summary of Key RCT Results for NightWare

Study	**Efficacy (Mean Change in PSQI-A ± SD)**	**Safety**
FDA De Novo Summary for NightWare (12)		
NightWare (change from baseline to day 30) (n=29)	-3.2 (± 3.7)	C-SSRS: -0.2 (± 0.8) ESS: -1.2 (± 4.1)
Sham (change from baseline to day 30) (n=34)	-2.2 (± 2.9)	C-SSRS: 0 (± 1.0) ESS: 1.2 (± 3.1)
p-Value	.26	C-SSRS: .29 ESS: .97

C-SSRS: Columbia Suicide Severity Rating Scale; ESS: Epworth Sleepiness Scale; FDA: Food and Drug Administration; PSQI: Pittsburgh Sleep Quality Index; PSQI-A; Pittsburgh Sleep Quality Index for PTSD-

associated sleep quality; PTSD: post-traumatic stress disorder; RCT: randomized controlled trial; SD: standard deviation.

Table 9. Study Design and Conduct Limitations for NightWare

Study	
FDA De Novo Summary for NightWare (12)	
Allocation[a]	3. Allocation concealment unclear; 4. Inadequate control for selection bias;
Blinding[b]	1. Participants or study staff not blinded (unclear) 2. Outcome assessors not blinded (unclear) 3. Outcome assessed by treating physician (unclear)
Selective Reporting[c]	
Data Completeness[d]	6. Not intent to treat analysis
Power[e]	1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference;
Statistical[f]	3. Confidence intervals not reported; 5. Other (unclear reporting on lack of achieving recruitment goal for trial: primary hypothesis, lack of control for type I error for multiple statistical comparisons)

The study limitations stated in this table are those notable in the current 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: Nightmare Disorder and Post-Traumatic Stress Disorder-Associated Nightmares

The evidence on NightWare includes a single trial that did not meet the primary efficacy endpoint. This trial failed to achieve recruitment goals and was likely underpowered. A well-designed blinded RCT with a clear design for testing a pre-specified hypothesis is needed. Given

these limitations, the benefit of NightWare in individuals with nightmare disorder and PTSD-associated nightmares is uncertain.

Summary of Evidence

For individuals with panic symptoms who receive Freespira, the evidence includes several single-arm studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Panic symptoms in individuals with panic disorder and post-traumatic stress disorder (PTSD) have been associated with more shallow and rapid breathing, and Freespira is intended to lead to more regular breathing through biofeedback over a 4 week training period. There are 2 single-arm studies in individuals with panic disorder and 1 single-arm pilot study on the use of Freespira in individuals with PTSD. All of the studies report an improvement in symptoms but are limited by loss to follow-up that ranges from 24% to 58% and multiple limitations in the design and conduct. A well-designed blinded randomized controlled study with a clear design for testing a pre-specified hypothesis is needed. Given the high loss to follow-up and lack of a control group in these studies, the benefit of a 4-week program of respiratory biofeedback in individuals with panic disorder and PTSD is uncertain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with nightmare disorder or PTSD-associated nightmares who receive NightWare, the evidence includes a single trial. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The single pivotal trial did not meet the primary efficacy endpoint. This trial failed to achieve recruitment goals and was likely underpowered. A well-designed blinded randomized controlled study with a clear design for testing a pre-specified hypothesis is needed. Given these limitations, the benefit of NightWare in individuals with nightmare disorder and post-traumatic stress disorder-associated nightmares is uncertain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

Veteran Affairs and Department of Defense Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Disorder

Clinical practice guideline for the management of PTSD were published in 2023. (14) Key findings and recommendations related to Freespira was limited to the following: "There is insufficient evidence to recommend for or against the following somatic therapies for the treatment of PTSD: capnometry-assisted respiratory therapy (Freespira)."

Health Technology Assessment: New York State Department of Health

The Health Technology Assessment commissioned by New York State Department of Health and prepared by Center for Evidence-based Policy Oregon Health & Science University published in November 2024 concluded the following: "Evidence related to Freespira was limited to a small number of non-comparative studies. These uncontrolled studies found that Freespira was associated with an improvement in symptoms of PTSD or panic disorder, it is not associated with serious adverse events, and the majority of patients are adherent to the

treatment protocol. However, our confidence in the evidence is very low for any of these findings, and we expect that adequately controlled research would change these findings. The limited number of trials, lack of control groups, small sample sizes, and high risk of bias should be considered when drawing conclusions about the certainty of evidence for Freespira for the treatment of panic disorder and PTSD. Overall, we have very low certainty in these results, and new research is likely to change our understanding of Freespira for panic disorder and PTSD." (15)

Ongoing and Unpublished Clinical Trials

Some currently ongoing and/or unpublished trials that might influence this policy are listed in Table 10.

Table 10. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT06419959	NightWare and Cardiovascular Health in Veterans With PTSD	125	Sep 2026
NCT07021014	NightWare and Cardiovascular Health in Women With PTSD	36	Jul 2028
NCT06399874	Nightmare Deconstruction and Reprocessing vs. NightWare Wristband (NDR/NW)	30	Mar 2026
NCT03934658[a]	A Remote Randomized Double-Blind Sham-Controlled Clinical Trial of NightWare in Adults With Post-Traumatic Stress Disorder and Co-Morbid Nightmare Disorder	400 (actual enrolled 81)	Dec 2021
NCT05365607[a]	NightWare and Cardiovascular Health in Adults With PTSD	40	Aug 2024
NCT04040387	Traumatic Nightmares Treated by NightWare (To Arouse Not Awaken) (TNT/NW)	15	Aug 2019

NCT: national clinical trial

[a] Denotes industry-sponsored or cosponsored 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	99199
HCPCS Codes	A9291, G0552, G0553, G0554

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

1. International Medical Device Regulators Forum. Software as a Medical Device (SaMD): Key Definitions. 2013. Available at: <https://www.imdrf.org > (accessed March 10, 2024).
2. National Institute for Health and Care Excellence (NICE). Evidence standards framework for digital health technologies. 2021. Available at: <https://www.nice.org.uk> (accessed March 10, 2024).
3. Deacon B, Lickel J, Abramowitz JS. Medical utilization across the anxiety disorders. J Anxiety Disord. 2008; 22(2):344-350. PMID 17420113
4. Meuret AE, Wilhelm FH, Ritz T, et al. Feedback of end-tidal pCO2 as a therapeutic approach for panic disorder. J Psychiatr Res. Jun 2008; 42(7):560-568. PMID 17681544
5. American Psychiatric Association. (2013). Trauma- and stressor related disorders. In Diagnostic and statistical manual of psychiatric disorders (5th edn)
6. Muhtz C, Yassouridis A, Daneshi J, et al. Acute panicogenic, anxiogenic and dissociative effects of carbon dioxide inhalation in patients with post-traumatic stress disorder (PTSD). J Psychiatr Res. Jul 2011; 45(7):989-993. PMID 21324483
7. Kellner M, Muhtz C, Nowack S, et al. Effects of 35% carbon dioxide (CO^2) inhalation in patients with post-traumatic stress disorder (PTSD): A double-blind, randomized, placebo-controlled, cross-over trial. J Psychiatr Res. Jan 2018; 96:260-264. PMID 29128558
8. Tolin DF, McGrath PB, Hale LR, et al. A Multisite Benchmarking Trial of Capnometry Guided Respiratory Intervention for Panic Disorder in Naturalistic Treatment Settings. Appl Psychophysiol Biofeedback. Mar 2017; 42(1):51-58. PMID 28194546
9. Ostacher MJ, Fischer E, Bowen ER, et al. Investigation of a Capnometry Guided Respiratory Intervention in the Treatment of Posttraumatic Stress Disorder. Appl Psychophysiol Biofeedback. Dec 2021; 46(4):367-376. PMID 34468913
10. Kaplan A, Mannarino AP, Nickell PV. Evaluating the Impact of Freespira on Panic Disorder Patients' Health Outcomes and Healthcare Costs within the Allegheny Health Network. Appl Psychophysiol Biofeedback. Sep 2020; 45(3):175-181. PMID 32342249
11. Morgenthaler TI, Auerbach S, Casey KR, et al. Position Paper for the Treatment of Nightmare Disorder in Adults: An American Academy of Sleep Medicine Position Paper. J Clin Sleep Med. Jun 15 2018;14(6):1041-1055. PMID 29852917
12. De novo classification request for Nightware kit (Apple iphone, Apple watch, Apple iphone charging cable, Apple watch charging cable). Available at: <https://www.accessdata.fda.gov> (accessed March 10, 2024).
13. Davenport ND, Werner JK. A randomized sham-controlled clinical trial of a novel wearable intervention for trauma-related nightmares in military veterans. J Clin Sleep Med. Feb 01 2023; 19(2):361-369.PMID 36305584

14. VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Disorder. Version 4.0-2023. Based on evidence reviewed through May 4, 2022. Available at: <https://www.healthquality.va.gov> (accessed on September 24, 2025).
15. New York State Department of Health: Health Technology Assessment. Freespira for Panic Disorder and Posttraumatic Stress Disorder. Published November 2024. Available at: <https://www.health.ny.gov> (accessed September 24, 2025).

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
12/15/2025	Document updated. Coverage unchanged. Added references 14 and 15; others removed.
11/15/2024	Reviewed. No changes.
11/01/2023	New medical document. The use of Freespira is considered experimental, investigational and/or unproven for all indications including treatment of panic disorder and/or post-traumatic stress disorder. The use of NightWare is considered experimental, investigational and/or unproven for all indications including treatment of nightmare disorder or nightmares from PTSD.

Appendix

DSM-5 Diagnostic Criteria for Panic Disorder

1. Recurrent and unexpected panic attacks
2. ≥1 attack has been followed by 1 month or more of one or both of the following
    a. Persistent concern about additional attacks or their consequences
    b. A significant maladaptive change in behavior related to the attacks
3. The panic attacks are not due to the direct physiological effects of a substance (e.g., a drug of abuse or a medication) or a general medical condition
4. The panic attacks are not better accounted for by another mental disorder.

DSM-5 Diagnostic criteria for Nightmares

1. Recurrent episodes of extended, extremely dysphoric, and well-remembered dreams that usually involve efforts to avoid threats to survival or security or physical integrity. The nightmares generally occur in the second half of a major sleep episode.
2. On waking from the nightmare, the individual rapidly becomes oriented and alert.
3. The episodes cause significant distress or impairment in social, occupational or other areas of functioning.
4. The symptoms cannot be explained by the effects of a drug of abuse or medication.
5. The nightmares cannot be attributed to another mental disorder (i.e., posttraumatic stress disorder, delirium) or medical condition.

DSM-5 Diagnostic Criteria for Post-Traumatic Stress Disorder (PTSD)

The following criteria apply to adults, adolescents, and children older than 6 years.

A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:
    1. Directly experiencing the traumatic event(s).
    2. Witnessing, in person, the event(s) as it occurred to others.
    3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
    4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains; police officers repeatedly exposed to details of child abuse). **Note:** Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.
B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
    1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). **Note:** In children older than 6 years, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed.
    2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s). **Note:** In children, there may be frightening dreams without recognizable content.
    3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) **Note:** In children, trauma-specific reenactment may occur in play.
    4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
    5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:

1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
    1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia, and not to other factors such as head injury, alcohol, or drugs).
    2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," "The world is completely dangerous," "My whole nervous system is permanently ruined").
    3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.
    4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).
    5. Markedly diminished interest or participation in significant activities.
    6. Feelings of detachment or estrangement from others.
    7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
    1. Irritable behavior and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects.
    2. Reckless or self-destructive behavior.
    3. Hypervigilance.
    4. Exaggerated startle response.
    5. Problems with concentration.
    6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).
F. Duration of the disturbance (Criteria B, C, D and E) is more than 1 month.
G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.

Specify whether:

With dissociative symptoms: The individual's symptoms meet the criteria for posttraumatic stress disorder, and in addition, in response to the stressor, the individual experiences persistent or recurrent symptoms of either of the following:

1. Depersonalization: Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly).

2. Derealization: Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted). Note: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (e.g., blackouts, behavior during alcohol intoxication) or another medical condition (e.g., complex partial seizures).

Specify whether:
With delayed expression: If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).