Prescription Digital Therapeutics

EOCCO POLICY

Policy Type:PA Pharmacy Coverage Policy: EOCCO283

Description

Prescription digital therapeutics (PDTs) are devices, internet applications or other software-based technology intended for the prevention, management, or treatment of a medical condition. PDTs are cleared, authorized, or approved under section 510(k), 513(f)(22), or 515 of the federal food, drug, and cosmetic act, and must be prescribed by a licensed healthcare provider. The purpose of this policy is to ensure the appropriate use of these interventions.

Length of Authorization

- Initial:
  - i. Somryst: one time authorization to cover up to 9-week treatment
  - ii. EndeavorRx: three months
- Renewal:
  - i. Somryst: not applicable; this is a single one-time treatment
  - ii. EndeavorRx: 12 months

Prescription Digital Therapeutics (PDTs) included in this Policy

Product Name	Indication	Quantity Limit
Somryst*	Chronic Insomnia	1 x access, up to 9-week treatment
EndeavorRx	Attention Deficit and Hyperactivity Disorder (ADHD)	One activation code/30 days

** Somryst NDC 96439-0030-01*

Initial Evaluation

I. **Somryst (digital therapy)** may be considered medically necessary when the following criteria are met:
   A. Member is 22 years of age or older; **AND**
   B. A diagnosis of **chronic insomnia**; **AND**
      1. Attestation by provider that all the following are met:
         i. Member is under their supervision; **AND**
         ii. Member is able to read and understand English; **AND**
         iii. Member is familiar with how to use mobile apps; **AND**
      2. Attestation by provider member's daily life or work does not require them to be highly alert or cautious (e.g., long-haul truck drivers, long-distance bus drivers, air traffic controllers, operators of heavy machinery, certain assembly line jobs)

II. **EndeavorRx** may be considered medically necessary when the following criteria are met:

A. Member is eight to 12 years of age; **AND**
B. Provider attestation that the requested Prescription Digital Therapeutic (PDT) is not prescribed primarily for the convenience of the member, caregiver, or the healthcare provider; **AND**
C. Provider attestation that the member does not have physical or medical restrictions to the use of EndeavorRx (e.g., photo-sensitive epilepsy, color blindness, physical limitations that restrict use of a mobile device); **AND**
D. EndeavorRx must be used in combination with conventional clinician-directed therapy (e.g., cognitive behavioral therapy [CBT], parent training in behavior management [PTBM], stimulant [e.g., amphetamine salts, methylphenidate] or non-stimulant [e.g., guanfacine, atomoxetine] pharmacotherapy); **AND**
E. Diagnosis of **Attention Deficit and Hyperactivity Disorder (ADHD)** when the following are met:
    1. Provider attestation that the member has primarily inattentive or combined-type ADHD with demonstrated attention issues; **AND**
    2. Documentation of moderate to severe ADHD as supported by a pre-treatment standardized assessment (e.g., Vanderbilt Assessment Scale, TOVA-API, ADHD-IRS, ADHD-RS-IV, CGI-S); **AND**
    3. Treatment with at least one of the following first-line therapies has been ineffective, not tolerated, or all are contraindicated:
        i. Clinician-directed behavioral interventions (e.g., Cognitive Behavioral Therapy [CBT], Parent Training in Behavior Management [PTBM])
        ii. Pharmacotherapy (e.g., stimulant [e.g., amphetamine salts, methylphenidate] or non-stimulant [e.g., guanfacine, atomoxetine])

II. Somryst and EndeavorRx are considered investigational when used for all other conditions, including but not limited to:
    A. Short-term insomnia
    B. Parasomnia
    C. When used as a stand-alone therapy
    D. Cognitive function improvement in disease conditions other than ADHD (e.g., autism spectrum disorder, systemic lupus erythematosus [SLE])
    E. Sensory processing disorder

Renewal Evaluation

Somryst:

Not applicable. Somryst is a one-time 9-week treatment.

EndeavorRx:

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member continues to use EndeavorRx in combination with other therapies (e.g., stimulant or non-stimulant medications, behavioral therapy); **AND**
IV. Documentation that member has exhibited improvement or stability of disease symptoms [e.g., improvement in Vanderbilt Assessment Scale, TOVA-API, ADHD-IRS, CGI-I scores]

Supporting Evidence

Somryst:

I. The American Academy of Sleep Medicine (AASM) strongly recommends cognitive behavioral therapy for insomnia (CBT-I) as part of the initial recommended approaches to treat chronic insomnia in adults.
    - CBT-I combines one or more cognitive therapies, alongside education about sleep regulation, stimulus control, and sleep restriction therapy. This can also include sleep hygiene education, relaxation training, and use of sleep diaries.
    - CBT-I is digitally delivered via the Somryst app on a tablet or smartphone.
II. While cognitive behavioral therapy is the standard of care in the treatment of insomnia, the FDA authorization of Somryst was based on a controlled study where CBT-I was delivered by a computer. Thirty-four subjects were randomized to receive either control (sleep diary) or computer-based CBT-I. The CBT-I treatment group had a statistically significant difference in improved sleep versus control.
III. Somryst is indicated in patients 22 years of age and older with chronic insomnia. Product claim includes improving insomnia symptoms.
IV. Somryst use is intended as a single 9-week treatment, under the supervision of a provider.
V. Somryst guides the user through various activities and modules over 6 to 9 weeks; there is no data to support repeat use or use beyond this time.
VI. Since CBT-I is delivered via a digital means on a tablet or smartphone, safe and typical use requires familiarity with apps and ability to read and understand English.
VII. Treatment with Somryst includes both sleep restriction and consolidation which can cause sleepiness, especially in the early stages of using this prescribed digital therapeutic. For individuals who must be alert or cautious to avoid serious accidents in their job or daily life, Somryst should not be used. Examples include: long-haul truck drivers, long-distance bus drivers, air traffic controllers, those who operate heavy machinery or select assembly line work.

EndeavorRx:

VIII. EndeavorRx (Akili Interactive Labs, Inc.) is an FDA-authorized Prescription Digital Therapeutic (PDT) indicated to improve attention function in children eight to 12 years of age with attention-deficit hyperactivity disorder (ADHD). Delivered via an action video game experience, one prescription of EndeavorRx provides 30 days of access and is administered daily (25 minutes, five days/ week).

IX. Utility of EndeavorRx has been assessed in the improvement of attention function as measured by computer-based testing in children ages eight to 12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue. During clinical trials, patients who engaged with EndeavorRx demonstrated improvements in a digitally assessed measure, (Test of Variables of Attention [TOVA]), of sustained and selective attention. Patients using EndeavorRx may not display benefits in typical behavioral symptoms, such as hyperactivity. EndeavorRx should be considered for use as part of a therapeutic program that may include clinician-directed therapy, medication, and/or educational programs, which further address symptoms of the disorder.

X. Although there are no contraindications noted to the use of EndeavorRx, this PDT may not be appropriate for patients with photo-sensitive epilepsy, color blindness, or physical limitations that restrict the use of a mobile device.

XI. Treatment recommendations for patients with ADHD vary based on age and include behavioral changes, cognitive therapy, and pharmacotherapy. Pharmacotherapy options include stimulants (e.g., methylphenidate and amphetamines) and non-stimulants (e.g., guanfacine, atomoxetine). The American Academy of Pediatrics (AAP) ADHD guidelines recommend parent training in behavior management (PTBM) and behavioral classroom interventions as the first-line treatment for children under 12 years of age. Additionally, for children six years and above, the addition of pharmacotherapy may be considered.

XII. EndeavorRx is the first PDT for the treatment of ADHD in children and was FDA-authorized via a *de novo* pathway. It may be considered an adjunct therapy combined with PTBM, clinician-directed behavioral therapy, and pharmacotherapy. EndeavorRx is not recommended to be used as a stand-alone therapy or as a substitute for pharmacotherapy. As of June 2023, The AAP guideline has not been updated to include EndeavorRx as a treatment option for ADHD.

XIII. EndeavorRx was assessed via two clinical trials, STARS-ADHD, a phase 3, randomized (1:1), double-blind clinical trial, which assessed response to EndeavorRx versus a digital sham control; and STARS-ADJUNCT, an open-label, dual-cohort trial which assessed EndeavorRx as an adjunct to stimulant therapy. STARS-ADHD included patients (N=348) aged eight to 12 years with baseline ADHD rating scale score (ADHD-RS-IV) ≥28, and Test of Variables of Attention - Attentional Performance Index (TOVA-API) ≤-1.8. Mean change in TOVA-API from baseline to day 28 was assessed as the primary outcome. STARS-ADJUNCT trial included patients (N= 236), eight to 14 years of age who were assigned to an on-stimulant cohort (n= 130) or a non-stimulant cohort (n=76). All patients had ADHD impairment rating score (ADHD-IRS) ≥3. Mean change in ADHD-IRS from baseline to day 28 was the primary outcome. A 28-day treatment during STARS-ADHD led to statistically significant improvement in TOVA-API for the trial

participants with a positive TOVA-API score 0.9 points higher in the treatment arm versus digital control (p=0.0060). STARS-ADJUNCT trial measured ADHD-IRS mean change from baseline to day 28, which reported a reduction of −0.7 (95% CI, −0.86, −0.50; *p* <0.001) in the on-stimulant cohort, and −0.5 (95% CI, −0.73, −0.32; *p* <0.001) in the non-stimulant cohort.

XIV. During STARS-ADJUNCT, exploratory secondary outcomes at day 84 (after a 28-day treatment pause), reported incremental improvement in ADHD-IRS (68.3%), ≥30% improvement in ADHD-RS (45.3%), and CGI-I scores ≤2 (27.6%) across both cohorts. Investigator-monitored compliance rates were 83% and 81% for STARS-ADHD and STARS-ADJUNCT trials, respectively. Additionally, both clinical trials reported patient-reported improvement in attention deficit (75%).

XV. Limitations of the clinical program for EndeavorRx include a narrow population age, exclusion of patients with psychiatric comorbidities, and short duration of intervention. However, both clinical trials reported consistent, statistically significant improvement in ADHD-related impairment and symptoms of inattention. TOVA-API is a validated tool of improvement in attention deficit and inhibitory control. Clinically meaningful improvements after three months therapy during STARS-ADJUNCT trial (ADHD-RS and CGI-I scores) provide additional indicators of efficacy. For the majority of pediatric patients with ADHD, when used as an adjunct therapy, EndeavorRx may serve as a practical intervention. Overall quality of evidence is considered low to moderate.

XVI. Overall, 12 (7%) and 37 (18%) participants experienced intervention-related adverse reactions (IRAEs) during STARS-ADHD and STARS-ADJUNCT, respectively. During STARS-ADHD, the most common IRAEs between the intervention versus digital control arms respectively, were decreased frustration tolerance (3% vs 0%), headache (2% vs 1%), and irritability (1% in each arm). For STARS-ADJUNCT, IRAEs were evenly distributed between the on-stimulants and non-stimulants cohorts, and included decreased frustration tolerance (13%), irritability (1.5%), headache (1.9%), and dizziness (1%). There were no serious adverse reactions reported. Three participants discontinued STARS-ADJUNCT due to IRAEs. Current safety data for EndeavorRx is limited to the clinical trial population and the real-world long-term safety remains unknown.

Investigational or Not Medically Necessary Uses

I. Somryst and EndeavorRx have not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Short-term insomnia
   B. Parasomnia
   C. When used as a stand-alone therapy
   D. Cognitive function improvement in disease conditions other than ADHD (e.g., autism spectrum disorder, systemic lupus erythematosus (SLE))
   E. Sensory processing disorder

II. EndeavorRx has been assessed in clinical trials for pediatric patients with ADHD and comorbid sensory processing disorder (SPD) as well as autism spectrum disorder (ASD). Results of these

clinical trials are not available as of June 2023. EndeavorRx has not received FDA-authorization for the above indications.

III. Additional clinical trial to assess the safety and efficacy of EndeavorRx in adolescent population (12 to 17 years of age) with ADHD is ongoing. In June 2023, EndeavorOTC, a non-prescription version of EndeavorRx, became available for use by adults (>18 years of age). EndeavorOTC is available as a downloadable software application (App) compatible with leading cellular phone operating systems and requires a monthly subscription fee. As of June 2023, the results of the clinical trial of EndeavorRx in the adult population are not available. Over-the-counter (OTC) devices and digital therapeutics may be considered excluded in accordance with the benefit designs for this health plan.

References

1. Somryst [Clinician Information]. Boston, MA: Pear Therapeutics, Inc. March 2020.
2. Feuerstein S, Hodges SE, Keenaghan B, Bessette A,Forselius E, Morgan PT. Computerized cognitive behavioral therapy for insomnia in a community health setting. J Clin Sleep Med. 2017;13(2):267-274.
3. Edinger JD, Arnedt JT, Bertisch SM, et al. Behavioral and psychological treatments for chronic insomnia disorder in adults: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021;17(2):255–262
4. Kollins SH, DeLoss DJ, Cañadas E, Lutz J, et al.. A novel digital intervention for actively reducing severity of paediatric ADHD (STARS-ADHD): a randomised controlled trial. Lancet Digit Health. 2020 Apr;2(4):e168-e178.
5. Kollins SH, Childress A, Heusser AC, Lutz J. Effectiveness of a digital therapeutic as adjunct to treatment with medication in pediatric ADHD. NPJ Digit Med. 2021 Mar 26;4(1):58.
6. Wolraich M, Brown L, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Pediatrics. 2011 Nov;128(5):1007-22.

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created (EndeavorRx) and combined with Somryst to create a Prescription Digital Therapeutics policy.	08/2023